THE EVOLUTION OF MODERN OBSTETRICS

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WHAT changes have there been in the attitude of women to childbearing, and what effect have these had on the maternity services? I shall here describe the evolution of the maternity services and the adjustments that seem necessary in the training of the medical student, the general-practitioner obstetrician, and the obstetric specialist.

The Mother

In 1861–69 the average family contained 6·16 children; by 1900–09 the number had fallen to 3·30; and in 1934–37 it was 2·04, the lowest on record. This coincided with a very low marriage-rate and the appointment of a Royal Commission on Population, which sat during most of the war years. Its excellent report aroused little general interest, since publication coincided with a post-war rise in the birth and marriage rates.

Marriage is now taking place earlier: for example, in 1957 55% of women in the age-group 20–24 were married, compared to 32% in 1938. Formerly, early marriages were associated with large families, but this is no longer so. It is estimated that when the women who married in 1952 have completed their childbearing the average family size will be 2·21 (Registrar General 1957). The fact that the average family size remains small despite the rising standard of living and early marriage makes it clear that most women now have children because they want them and not because they cannot prevent pregnancy. The improved health and growth of young mothers should help to ensure that reproductive wastage is kept to a minimum.

The attitude of women to the discomforts of labour seems more balanced than it was. They recognise that labour is less of a trial if they adopt a calm and confident approach to childbirth encouraged by sympathetic doctors and midwives. But at the same time they expect as much relief as possible from unnecessary suffering. Obstetricians and anæsthetists have responded by devising better methods of relieving pain, and there is no doubt that the standard of anæsthesia and analgesia has improved remarkably in the last ten years.

But the change in reproductive habits brings its own problems when plans go wrong. Parents in all social classes are much more ambitious for their children than formerly, as is indicated by the much larger numbers coming forward for secondary and university education and the much bigger proportion coming from " working-class " homes. When an unwanted pregnancy occurs, the emotional upset is often greatest in those who are most ambitious for their children. Such women need a great deal of help, and occasionally a heaping-up of circumstances may drive a woman to breaking-point, so that termination of the pregnancy may be necessary. Again, there are still many women who are worn out by repeated pregnancies. Often of poor physique initially, especially those living in the slums of our large cities, they seem incapable of avoiding pregnancy. Although maternal mortality is relatively high amongst them, they are characteristically much less disturbed emotionally by an unwanted pregnancy than women with more education and higher ambitions. Since contraceptive advice is more or less useless in such cases, sterilisation should be used much more frequently, and in my experience it is welcomed. Used with discretion, postpartum sterilisation can greatly improve the physical and mental health of the mother and the general wellbeing of the family circle, and is therefore good preventive medicine.

The Services

Just after the first world war most confinements took place in the home. Since the 1911 National Health Insurance Act did not provide for the medical care of mother and child, a doctor was not freely available and many women could not afford a medical fee. To fill the gap, the Government, through the local authorities, set up antenatal clinics, and by 1935 there were about 1400 State-aided clinics in England and Wales. In some voluntary hospitals, part or all of the cost of treatment of both antenatal outpatients and inpatients was borne by the local authorities. This service has helped to raise the standard of antenatal and child care to its present high level. Now that every mother has a family doctor, the future of the maternity and child-welfare service is in doubt; but any attempt to dispense with it at present would be dangerous, since most practitioners have neither the time nor the facilities for health education. The great pressure on his time would force the practitioner to neglect the educational and preventive aspects of his work because of the more pressing need to treat illness and disease. One hopes that this may be remedied and that in the future the family doctor will play a bigger part in preventive medicine.

In the 1920s the training of the family doctor in midwifery was very unsatisfactory and he had to learn from experience under most unfavourable conditions. Some measure of the low standard of obstetrics was the frequency of what was known as the " failed forceps outside " type of case. In the years 1925–34, 426 cases were admitted to the Glasgow Maternity Hospital after an unsuccessful attempt by the general practitioner to deliver with forceps in the patient's home. The maternal mortality was 14%. During the years 1932–34, 167 " failed forceps " cases were sent in by 121 practitioners. 95 doctors sent one case each, but 3 doctors were together responsible for twenty cases, and one of them sent in a total of 9 cases in the three years. This doctor had acquired the reputation, in the poorer parts of the city, of being able to deliver the baby with the minimum delay when sent for by the tired midwife.

It must be pointed out, however, that failure to deliver the baby with forceps occurred inside the hospital as well as outside, sometimes even in booked cases. During 1925–34, 373 craniotomies were performed with a maternal mortality of 9%. These deplorable figures may to some extent be excused if it is remembered that cæsarean section in such cases carried an even higher death-rate.

Maternity Hospitals

In the inter-war years our maternity hospitals were seriously defective. Their size and number were determined not by the needs of the community but by the money available. In sharp contrast to children's hospitals, maternity hospitals have always found it difficult to attract donations of money from the public, perhaps because many were founded originally primarily to care for unmarried and destitute mothers. Thus, many of our leading maternity hospitals were, and still are, overcrowded, ill equipped, and in some respects dangerous places. Antenatal clinics attached to the hospitals are often equally defective. When they were planned there was no appointments system and little waiting accommodation; it was a common sight to see expectant mothers queuing in the street for an hour before the doors opened.

The obstetricians attached to such hospitals comprised all the leading teachers in the country, but their professional outlook was, with a few exceptions, restricted to the technical details of operations and the internal affairs of the hospital. The wider problem of the needs of the area and of the services required to meet them was not their responsibility. The effect of this restriction of outlook can still be seen in the form and content of the annual medical reports which are compiled by most leading maternity hospitals. These reports contain little more than a list of abnormal cases treated and the outcome for the mother and child. The results of treatment vary greatly with the type of patients treated, the kind of community in which the hospital is situated, and whether the cases are booked or emergency, and on the proportion of each. Consequently, conclusions regarding the effect of treatment are difficult to draw and comparison of the results from different hospitals are often very misleading. Even comparisons of the results in the same hospital over a period of years may be misleading because of general factors whose influence cannot be measured. What is wanted is an analysis, on sound epidemiological lines, of all the births in a region.

There has been a steady drift towards hospital confinement. In England and Wales in 1925, 15% of live births took place in hospital; by 1937 it had reached 40% and by 1957 65%. In Scotland, since 1948, the teaching hospitals have been an integral part of the regional hospital service. This has allowed planning of a regional maternity service, with the teaching hospital as the central point of the service in each area. The importance of having the university departments of child health, preventive medicine, and obstetrics linked closely to the hospitals and to the public health service cannot be overstated. It has been argued that the staff of the teaching hospital will dissipate its time and energy by such a process, but I am sure that the danger can be avoided by adequate staffing and proper delegation of duties. The advantages to the universities are very great because clinical teachers have an opportunity to gain a wide perspective. At the same time, the universities have the duty as well as the opportunity of acting as leaders in advancing the standard of medical care. They can work in close association with consultants and other members of the obstetrical staff of the hospital, so that the organisation of the maternity services, methods of treatment of patients, and training of undergraduates and postgraduates can be planned and integrated.

The fact that the stillbirth-rate in the City of Aberdeen in 1957 is little more than a third of the rate in 1937 is partly due to the fact that the staff of the university department is closely integrated with the National Health Service staff, and is able to supply the stimulus necessary to maintain a high standard of care, to conduct research, and to test scientifically any new method of treatment suggested by research. Another factor is the increase in the incidence of hospital delivery from 30 to over 80% during the period. Since all the maternity beds in the city are in the teaching hospital, the problem of ensuring a uniformly high standard of obstetric care is simplified. Another very favourable factor in Aberdeen has been the great help and cooperation given by the medical officer of health and his staff of midwives, health visitors, and maternity and child-welfare officers. As a result the educational and preventive aspects of midwifery have been thoroughly taught, and overlapping of effort has been avoided. Detailed statistical analysis of all births in the city, irrespective of the place of confinement, is made annually. An accurate picture of progress is therefore available, and the measures necessary for further progress can be discussed on the basis of numerical fact. Whatever modifications may be introduced in the future, there is no doubt that the present method of organisation has reduced the perinatal mortality more quickly than would have been possible in any other way.

The organisation of a maternity service is peculiarly difficult for two reasons. Firstly, it is impossible to tell when labour will start, so that a fully staffed service, irrespective of the load of cases, must be maintained night and day; and secondly, the onset of many serious complications of pregnancy and labour is unexpected and sudden, so that special facilities must be constantly available at short notice. Hence only a large maternity hospital can be fully competent to deal fairly economically with all eventualities.

A local maternity service in towns and cities should therefore be built round a centrally placed maternity hospital which should take all primigravidæ, all potentially abnormal multiparæ, and all those who require hospital confinement for social reasons. Very large cities should be divided into sectors with a maternity hospital at the centre of each. In Aberdeen we are fortunate enough to be able to admit not only those women for whom hospital confinement is desirable but also those who prefer to be confined in hospital. We can therefore avoid distasteful selection of cases and the unhappiness caused by it. Some women prefer to have their babies at home; for them the domiciliary service of general-practitioner obstetricians and midwives is available, but the hospital service must be able to give effective help when an emergency arises.

While there is much to be said for making a large maternity hospital the central point of the maternity service, it is not a good plan to concentrate all antenatal and postnatal clinics in the centre. The normal patient should attend a clinic in her own area which works in close association with the child-welfare clinic. In this way the patient comes under the influence of the child-welfare department. Health education can be given both at the clinic and in the patient's home. An obstetrician from the central hospital can attend at regular intervals to take part in the antenatal care. It may be possible to arrange that selected general practitioners take a large amount of the work at such clinics. Abnormal cases are best seen at an outpatient clinic at the hospital centre, where special investigations can readily be made and a consultant's opinion obtained.

In domiciliary midwifery in the poorer parts of large

cities general practitioners and midwives have to contend with poor facilities and with lack of intelligent cooperation from many of their patients. Many doctors work in isolation and are not accustomed to discuss their problems with colleagues. This is in marked contrast to the state of affairs in hospital, where more and more the emphasis is on team-work, with free discussion of methods of treatment and constant appraisal of the results of treatment. Domiciliary confinement is no doubt psychologically helpful to many mothers, but the advantage from the point of view of safety is certainly with the well-equipped and well-run hospital. Good running of a hospital naturally includes treating the patient as an individual and with kindness as well as at a high level of technical efficiency.

Many general practitioners are now in favour of hospital delivery and a demand for general-practitioner beds in hospitals is growing. In country districts, because of the distances involved, the general practitioner must take a great measure of responsibility for the work in the local maternity hospitals. But he should be helped by the visiting specialist, who is ultimately responsible to the regional hospital board for the standard of work in these small units. In the cities, general-practitioner beds may be attached to the teaching or base hospital as the case may be, and again the practitioner should work in close contact with the specialist team and take part in staff discussions, especially if one of his own cases should come under review. It is unrealistic to insist that the consultant should be called in only when requested by the general practitioner; the consultant should be free to keep in touch with practitioners on his own initiative, and to give informal advice when he feels it is necessary.

While much of antenatal care is within the competence of any conscientious family doctor, operative obstetrics cannot be taught to all medical students. For operations such as surgical induction, delivery by forceps, or the repair of vaginal lacerations the doctor must acquire his skill after graduation, as a resident house-surgeon in a maternity hospital; and this skill must thereafter be maintained by regular practice. A general practitioner cannot have regular and sufficient experience of obstetrics unless he is attached to, or becomes a member of, a fairly big group practice where each member of the group has a special interest and acts as the link between his colleagues and the specialist in that particular branch of medicine—in this case, the obstetrician and gynæcologist.

Administratively, the maternity services in Britain are untidy; the Guillebaud Committee went so far as to say that they are in a state of confusion. But the Cranbrook Committee in England and the Montgomery Committee in Scotland thought that the tripartite structure of the maternity services should be retained, because it would not be practicable to transfer the maternity services alone to hospital control when all other health services remain tripartite. The Cranbrook Committee proposed that local maternity liaison committees with a professional membership should be formed to ensure that local provision for maternity care is utilised to the best advantage. Local clinical meetings should be encouraged so that all persons in an area responsible for carrying out maternity care can discuss the clinical aspects of maternity cases. The Montgomery Committee thought that area professional advisory committees might be set up to make recommendations as to how the service could be coordinated and improved at the professional level.

Both committees thought that a minimum of 70% of hospital confinement would be a reasonable aim in Britain. There are great differences throughout the world in the incidence of hospital confinements. In many of the highly developed countries, particularly in the U.S.A. and Scandinavia, the proportion of women delivered in hospital is very high—e.g., 96% in Sweden. In Holland, on the other hand, hospital delivery is only about 30%. The stillbirth-rate is very little higher in Holland than in Sweden, and both are low by British standards. The Dutch example shows that given a very well-organised maternity service and a very high standard of physique and health of expectant mothers, and certain other favourable environmental and social conditions, it is possible to have a safe and efficient domiciliary service.

In some of the less industrialised regions of England, the perinatal mortality is reasonably low though only about half the deliveries take place in hospital. In the heavily industrialised areas, on the other hand, it is generally high, irrespective of the proportion of hospital deliveries. For example, in Wales in 1957 it was 44 per 1000, despite a hospital-delivery rate of 67%. In such areas, the home conditions are often unsuitable for delivery because of overcrowding, poor water-supply, and lack of other amenities; in addition, because the health and physique of mothers tends to be poor, complications of pregnancy and labour are frequent and serious.

The mere fact that delivery takes place in hospital does not ensure that all will be well, but it does lessen the risk. It is particularly important to have enough beds for antenatal complications and the number required increases as the level of health of the community declines. In Aberdeen, we have calculated that 8 antenatal beds per 1000 deliveries are required, and about a third of all cases booked for confinement are admitted for treatment at some stage of pregnancy. Many women in the city, especially multiparæ in the lower social classes, would benefit greatly in health if they were relieved of some household duties towards the end of pregnancy. Their improvement during a short stay in hospital is often quite striking, but some simpler form of accommodation in a hostel or convalescent home would be sufficient. If there is an overall shortage of beds, it may be better, as suggested by Theobald (1959), to discharge suitable patients to their homes early in the puerperium, rather than reduce the beds available for antenatal cases.

Medical Education

Undergraduates

Only a proportion of doctors will practise obstetrics and only those who have had postgraduate experience should do operative obstetrics. We should therefore concentrate on giving students a broad view of the problems of human reproduction and spend less time on the management of abnormalities in labour.

The student should have a clear understanding of the physiological changes of pregnancy—the influence of heredity and environment on reproduction; the influence of age, emotional factors, and customs on reproduction and on sex function in general. The problems of health education, preparation for marriage, and family planning should also be considered. He should, of course, understand the mechanism of labour and the various abnormalities which occur, but it is not possible to give him enough practical experience to become skilful in the procedures which sometimes become necessary even when uncomplicated delivery has been expected. The purpose of undergraduate training, in short, should be

to turn out a man who knows the " natural history " of human reproduction and who can take a comprehensive view of the general as well as the medical problems of having a family. He should not, however, be led to consider himself fully equipped, without postgraduate training, to undertake obstetric practice.

Postgraduates

General-practitioner obstetrician.—The family doctor who wishes to take full responsibility for his patient during labour as well as during the pregnancy should hold a resident post in a maternity hospital for six months, after which he should be competent to repair a torn perineum, deliver with forceps, and remove a placenta manually. He should then be encouraged to take the diploma in obstetrics of the Royal College of Obstetricians and Gynæcologists. This type of training should lead to a high standard of obstetrics amongst general practioners, especially if general practice is organised so that the well-trained practitioner can remain up to date and efficient.

Obstetric specialist.—Twenty-five years ago there were few paid training posts even in the leading teaching hospitals, and no recognised system of instruction of specialists existed. Consequently the standard of clinical practice varied greatly. The Royal College of Obstetricians and Gynæcologists, since its foundation in 1929, has done much to improve the training of specialists, not only by holding examinations but by laying down standards of practical training. As a result the standards of obstetric practice have been raised throughout the country as a whole to a high level.

Till the advent of the National Health Service almost the only goal for the young obstetrician was a busy private practice, yielding a good income and an interesting and varied professional life in which teaching often accompanied clinical work. But the obstetric specialist, especially if he is attached to a teaching centre, can no longer afford to concern himself solely with hospital routines and with building up a private practice. He should also be responsible for advising on regional needs, for raising standards of treatment by non-specialists, for relating the teaching of obstetrics to modern requirements, and for fostering research. The increasing store set by the community on health demands a high degree of technical skill from the specialist, and amid changing conditions he also needs breadth of outlook, foresight, and adaptability. He who wishes to lead in his field cannot afford to neglect science and the inculcation of the scientific spirit of inquiry. We are still familiar with the specialist who emphasises that he is a clinician not a scientist, suggesting that the two ways of life are mutually exclusive. In the conditions of private practice research has been almost impossible owing to lack of time and facilities, and even in hospital the specialist's time is fully occupied with the care of many seriously ill patients who require urgent treatment.

Those consultants who have been brought up under the old system lay stress on the value of private practice as a training, since it allows the consultant to take more interest in the patient as an individual, brings him more into contact with the family doctor and the patient's home, and thus gives him more insight and understanding. In hospital, because much of the treatment is given by house-surgeons and registrars, he may have little opportunity to talk to the patient alone. There is a tendency for the patient to become a case, and the importance of considering her illness in relation to her home background may be overlooked. Hospital treatment need not be impersonal; but with a relatively small staff, and a large number of patients to be treated, it is not easy to organise work so that continuity of treatment by one person is assured. Nevertheless an atmosphere which is acceptable to patients can be inculcated if medical and nursing staffs work as a team, if consultants set an example of sympathetic understanding of the patient, and if case-records are so detailed that even a " new " doctor can approach a patient knowing a good deal about her as a person. Under such conditions the patient develops confidence in the staff of a hospital rather than in an individual doctor or midwife.

Medicine is advancing so rapidly, methods of investigation are becoming so complex, and the standard of treatment is becoming so high that the system which served well in the past will not suffice in the future. The great need today is to maintain contact with the various other branches of medicine. Obstetricians need help in some aspects of radical surgery, medical complications of pregnancy, radiotherapy, the care of the newborn, obstetric anæsthesia, genetics, sociology, and psychology. They also need help from the scientific departments of physics, biochemistry, and physiology.

Research

Under the present system of specialist training, research is not essential, and is, indeed, made very difficult because of the need to amass experience, study textbooks, and sit examinations. The examination system tends to favour the orthodox, whereas research is essentially an adventure, in which imagination, the critical faculty, and even heterodoxy are at a premium. In this respect, research has much in common with the creative arts. The newly fledged M.R.C.O.G. is likely to be at least 30 before he is free from an imposed regime, and experience indicates that unless a man is given a taste of research before this age, it is difficult to get him started.

The earlier obstetricians were preoccupied with the problems of difficult labour. When labour came to a standstill how was one to get the baby delivered? To solve this problem, the Chamberlens invented, and a long line of successors improved, the obstetric forceps. Numerous manipulations were devised to manœuvre the fœtus into the most favourable position for delivery and instruments such as perforators and cranioclasts were invented to destroy it when necessary in the interests of the mother. The problem of difficult labour, taken together with the operative nature of most gynæcological treatment, explains why the outlook of the obstetrician and gynæcologist has long been dominated by surgery and why it has usually been considered necessary to take an F.R.C.S. as well as the M.R.C.O.G. With better diagnosis and good cooperation from surgical colleagues it is less essential, in the large teaching centres at least, for the obstetrician and gynæcologist to be an expert general surgeon.

The main problems today are medical and physiological rather than surgical. The origins of pre-eclampsia and eclampsia—the main causes of maternal mortality—are as mysterious as those of puerperal sepsis half a century ago. To uncover them, the obstetrician needs a sound knowledge of the hypertensive and renal diseases, and of the factors which alter water and electrolyte metabolism. Prematurity has replaced birth trauma as the main cause of perinatal mortality, and, although the management of the liveborn premature has improved, we know little about the reasons why fœtal growth is impaired or why

labour starts, whether it be at term or very much earlier. The pathologist is often unable to determine the causes of stillbirth and neonatal death. Even if the necropsy shows that the immediate "cause" was asphyxia, atelectasis, or immaturity, it cannot show *why* the baby was asphyxiated or was born immature. Few standard textbooks of obstetrics or physiology have much to say about human reproduction after they have dealt with fertilisation and the endocrine changes of early pregnancy; yet there are many clinical phenomena which demand study by physiological methods.

For example, the average mother puts on twice as much weight during pregnancy as can be accounted for by the fœtus, placenta, and liquor amnii. What is the nature, explanation, and purpose of this disproportionate gain? What happens if the mother gains much more or much less than the average amount? Does the wellbeing of the fœtus depend mainly on the nature and quality of the diet taken by a pregnant woman or can it ensure its own survival by growing when necessary at the expense of the maternal tissues?

Psychology and sociology are also growing in importance in relation to obstetrics. Reference has already been made to some of the problems of family planning in modern society. Much has been written in recent years about "natural childbirth". It is claimed that the confident, relaxed mother will have an easy and painless delivery compared with that of a worried, tense mother. Is this true, or merely an exaggeration of the axiom that the kindly obstetrician will gain the patient's confidence, so that she can face the ordeal of labour in a cheerful frame of mind, caring more about the happy outcome than the present pain?

Few practising clinicians can hope to become masters of the more specialised skills needed for intensive study of biological and sociomedical problems. But this does not mean that research is beyond the capacity of the clinician. Indeed, the clinician is better qualified than anyone else to undertake the systematic study of ordinary clinical records. The value of such study is unquestionable. By it, he can assess results, discover trends, and improve treatment. By appealing to numerical fact instead of to subjective impressions, he can sharpen clinical judgment and improve the standard of observation in the wards and operating-theatres.

As in all other fields of investigation, clinical study on these lines should be properly organised and should make use of reliable and efficient techniques. In too many hospitals the records system is run by an officer whose contacts with clinicians are administrative only, or by a succession of young obstetricians in training. As *The Lancet* (1960) noted, "the consultants must set the standard and be prepared to supervise the quality of the case-note taking, and themselves take part in transcribing medical information from the case-notes into the records system". They are more likely to do this willingly and intelligently if they themselves use the records system for the purposes of research.

In Aberdeen, we have gradually improved our standard of taking case-notes, and a statistical section forms an essential part of our research team. We have compiled accurate statistics relating to all births in the City of Aberdeen since 1948, and our assembly of classified records covering the whole of a defined population is probably unique in its scope, flexibility, and accuracy. Any reputation we have gained as a centre of epidemiological research is based primarily on the painstaking collection and organisation of thousands of facts by an interested team of senior obstetricians, aided by the staff of the records office of the hospital and the statistical section of the Obstetric Medicine Research Unit.

But the study of routine clinical records is clearly insufficient in itself, and a university department has an obligation to apply laboratory and other techniques to the study of obstetric phenomena.

We may agree that obstetricians should themselves participate as far as possible in studies involving specialised methods, but they can rarely hope to compete effectively with professionals in the various fields. Very few obstetricians have the aptitude and the opportunity —let alone the courage—to step aside from their specialty for a few years in order to be thoroughly trained in a basic science, such as biochemistry. For effective research involving biochemistry, obstetricians should therefore seek help from professional biochemists, and similarly with other fields.

In Aberdeen, over the past fifteen years, we have built up a team which at the moment includes 19 graduates engaged entirely or partly on research. Of the 19, 7 are obstetricians. 5 others are medically qualified but not specialist obstetricians; they include a physiologist and an epidemiologist with special experience in nutrition. 7 members of the team are not medically qualified; they include 2 chemists, a statistician, and a group engaged in sociological studies.

The formation and direction of a mixed team such as this poses many problems quite apart from those of earning and retaining the confidence and support of bodies willing to finance research. If they are to be effective, non-medical graduates working in a clinical department must be given a great deal of independence and a status equal to that of their clinical colleagues. It is very easy for a scientist in a clinical team to feel an outsider, both professionally and socially. Indeed he *is* an outsider in the sense that he has probably stepped off the usual ladder to promotion and advancement in his own specialty. If he is not sufficiently experienced to direct his own work, he rapidly loses perspective. If, on the other hand, he knows what is needed and is given the freedom to pursue the line that seems best to him, his clinical colleagues will need to be receptive to unfamiliar lines of thought and they must also give him the active support and help he requires in extracting information or biological materials from patients. Teamwork, which is so necessary for progress under modern conditions, involves more than mere collaboration, and its growth is rarely spontaneous. Experts with a diversity of skills and technical languages must be induced to talk and to work together, day by day, so that they will develop bonds of mutual interest and understanding.

Reproductive life in the human species is a lengthy process, and for the solution of many problems research over a long period must be undertaken. This means that a research team should not be regarded as an ephemeral affair to be supported by a patchwork of financial grants and administrative expedients. If they are to concentrate on biological problems, whole-time research-workers should not be continually preoccupied by the problem of making a living and obtaining promotion. Thus, it becomes necessary to guarantee careers, with adequate security and remuneration, for research-workers who have won their spurs.

During the past decade, the Medical Research Council has greatly eased problems of this nature by its enlightened

policy with regard to clinical research, and by forming numerous permanent research units of which the Obstetric Medicine Research Unit in Aberdeen is one. The unit is housed partly in the university department of midwifery and partly in special accommodation forming an integral part of the Aberdeen Maternity Hospital and built with funds given to Aberdeen University by the Scottish Hospital Endowments Research Trust. With this physical setting, and with a common directorship, the university, hospital, and M.R.C. staffs are able to work very closely together as a team.

It will surely be a step in the right direction if more obstetricians are trained in the outlook and methods of research, preferably by working for a period in a team such as this. The first need is to adjust the training of the obstetrician to modern requirements by reducing the emphasis on general surgery and by encouraging the growth of medical and physiological skills, preferably in a research setting. Beyond that, there is a need to lower the hurdles which make most obstetricians fear for their future if they leave the orthodox path of progression from house-surgeon to consultant. I feel sure that the academically minded obstetrician, given an adequate training in research methods, and proper facilities to undertake clinical research, can make important contributions to knowledge, particularly if he is prepared to make research the focus of his career. Several physicians have done this, and a few surgeons; but almost no obstetricians. Yet I cannot believe that in obstetrics we are willing to leave scientific progress mainly to the efforts of others.

Conclusions

Great progress has been made in obstetrics during the past twenty-five years. Much of this has followed the application of specific discoveries, but there have also been advances in clinical technique and in the organisation of the maternity services. With a rising standard of living, the health, nutrition, and level of hygiene of the population have improved. Better-educated parents have taken full advantage of the services provided, and now take steps to plan their families so that they can bring up their children well.

These scientific and social changes have been accompanied by a dramatic reduction of maternal mortality; but perinatal mortality, after responding in a striking manner before 1948, has, in England and Wales, been almost stationary during the past decade, at about 36 per 1000 births.

We may expect that continued social improvement, with an earlier average age at the birth of the first child, will of itself result in a gradual fall in the perinatal death-rate. But there is evidence that a higher standard of obstetrics could quickly lower perinatal mortality in areas where it is now above average. Where a rate of 30 or less has been reached, present methods of treatment have probably almost reached their limit of usefulness.

To ensure further progress, an ever greater rise in the level of maternal health and physique will be necessary. And to deal effectively with the disorders of pregnancy that arise in a generally healthy population the obstetricians of the future will need to know more about the physiology of pregnancy and the meaning of the variations of efficiency associated with age, parity, and physique. The significance of factors such as these is ultimately bound up with the social context and environment in which women live. Therefore, the leaders in the field of obstetrics must not only be good physiologists, physicians, and surgeons; they must also know something of sociology and psychology, and of vital statistics. This widening of the field of obstetrics to cover all aspects of human reproduction should attract enough entrants of the high calibre necessary to ensure further progress in this uniquely interesting branch of medicine.

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A CHEMICAL AND BACTERIOLOGICAL STUDY OF GALLSTONES

THE PRESENCE OF AN ACTINOMYCETE

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CHEMICAL analysis has been the means of inquiry into the cause of gallstone formation for over a hundred years (Thomson 1833). By the 1890s knowledge concerning gall-bladder disease was sufficient to allow the publication (1892) of a monograph by Naunyn entitled *A Treatise on Cholelithiasis* wherein is expounded a theory—namely, that many of the stones in which cholesterol and bile-pigments are mixed originate from those pultaceous masses of biliary debris which are sometimes found in the diseased gallbladder. A crust of cholesterol forms around each mass and by crystallisation inwards gradually transforms it into a stone (cholesterinisation), thus accounting for the soft friable centres of some " mixed " stones. Other kinds of gallstones have a hard centre, and Naunyn believed that these started as a nucleus of calcium bilirubinate in the same way as pure pigment stones. Rovsing (1924) was to postulate that all types of gallstones are formed around such a central nucleus of pigment, which in its turn is derived from a minute cast of the hepatic canaliculi, formed as a result of hepatic dysfunction and then carried in the bile to the gallbladder.

The primary cause of the chemical changes by which stones are formed, however, was considered by Naunyn and his contemporaries to be the result of inflammation of the wall of the gallbladder, a " lithigenous catarrh ". The new science of bacteriology had opened up the way for investigation in this field (Gallippe 1886). It was found that normal bile is sterile. In acute cholecystitis, organisms such as the coli-typhoid group could be isolated. By 1890 Welch (according to Cushing, 1898) had isolated *Bacillus coli* (*Escherichia coli*) and then typhoid bacilli from gallstones. Richardson (1898) observed the " clumping " of the bacilli in the bile in typhoid cholecystitis, a phenomenon suggestive of a gigantic Widal reaction within the gallbladder.

Thus the emphasis of research into gallstone formation was put upon the hypothesis that blood-borne organisms, such as *E. coli* and *Bacillus typhosus*, reached the wall of the gallbladder and then by the exfoliation of inflammatory cells, the production of abnormal protein and their actual presence in the bile caused the centre of stones to form. Gilbert and Fournier (1897) demonstrated in animals that stones could be formed after the intravenous injection of attenuated cultures of typhoid bacilli. Following the same pattern of research Rosenow (1914), Wilkie (1927), and Illingworth (1927) showed that the most commonly found organism in the wall of the gallbladder and cystic gland was the streptococcus or *E. coli* and that stones could be formed experimentally after intravenous injection of these organisms (Rosenow, Wilkie). Cholecystitis, among many other diseases, appeared to be due to a bacillæmia caused by some focus of infection in the body and it was popular to blame the teeth, the tonsils, and the paranasal sinuses as well as the colon, the cervix, and the prostate.

These experiments mainly concerned the cause of cholecystitis rather than the primary cause of gallstones, and the isolation of organisms from the centre of stones was not pursued with such zeal. In 1936, Helström, in Sweden, was investigating renal calculi and found staphylococcus within their matrix. In the same country, Martensson (1941) published a very comprehensive treatise on the formation of gallstones and drew attention once more to the organisms to be found in stones. By direct smear and culture he isolated what he called a "typical" bacillus—one with pleomorphic and subtilis-like characteristics. Following the usual pattern of experiment by inoculation stones were formed in the gallbladders of rabbits.

Programmes of research often involve repetition of the investigations of others. In this department the search for the causal phenomena of gallstones has required such studies. Thus we are presenting some results of the chemical analysis and the bacteriological study of the stones, our attention being particularly focused on the stone centre or "nucleus". Originally a pilot and macroscopic survey of stones had suggested that Rovsing's theory might be correct.

Methods and Results

For the purpose of the chemical and bacteriological study of stones from 57 patients it was decided to bisect each stone, after flaming, in the bacteriology department and to prepare first the microscopical specimens and the cultures from one half before proceeding to analyse the other half chemically. Thus the bacteriological techniques and results are mentioned first. Methods and results of chemical analysis will then be considered.

Bacteriological Techniques and Results

Examination of the 57 specimens of gallstones submitted for bacteriological examination (to G. J. B. and J. F. D. S.) has yielded 30 isolations in pure culture of an actinomycete (fig. 1). This organism grew only very slowly in primary culture under strict anærobic conditions, requiring from 10 to 87 days' incubation before it appeared in the preparations made from the original meat-broth cultures. By reason of the findings the bacteriological work required is extensive and associated with many complex problems. As this is, in some degree, a preliminary report we (G. J. B. and J. F. D. S.) shall not here describe all our techniques in detail, but confine ourselves to the two on which our present work has been based.

Preparation of microscopical specimens from gallstones.—A drop of sterile plasma, which has been filtered through a bacterial filter, is placed on a clean grease-free microscope slide, and small flakes of a gallstone to be examined are placed on it and then ground to a paste with a sterile platinum loop or needle. The paste is then spread thinly and evenly on the slide, is air-dried, and is then fixed with methyl-alcohol and stained by Gram's method (fig. 2).

Fig. 1—Preparation from anaerobic culture of gallstone showing branching and pleomorphic actinomyces.

Preparation of agglutinating suspensions of actinomyces.—A pure culture of the organism is transferred to 3 tubes of glucose broth which are incubated anaerobically at 37°C for seven days. The cultures are then centrifuged and 0·5 ml. of 0·01 *N* sodium carbonate and a trace of powdered trypsin (enough to cover a knife-point), are added to the pooled deposit from the cultures. The mixture is incubated at 37°C for eighteen hours in a sterile tube closed with a rubber bung. After this incubation, 1 ml. of acid alcohol (5 parts *N* HCl to 95 parts of absolute alcohol), is added to the mixture, which is then allowed to stand for three to five minutes at room-temperature. At this stage precipitation of the bacterial protein occurs and is visible as a flaky deposit. This deposit is now centrifuged and washed in several changes of sterile saline (0·85%) by rapidly decanting the supernatant saline and adding fresh saline between successive centrifugings. This process results in the production of even suspensions of the organisms which are satisfactory for agglutination tests. Our agglutination reactions have been performed at a temperature of 40°C acting for eighteen hours, before the results are read.

Serological Character of the Actinomyces

Table I shows that the actinomyces isolated from the stones are homogeneous in their serological characters, when tested against experimental immune rabbit sera, and that they differ distinctly in such serological characters from *Actinomyces bovis* of Wolff and Israël.

Chemical Analysis and Expression of Results

After bisection and bacteriological sampling of the stones, drawings were made of each of the 57 specimens to show the appearance of the sectioned surface. Details

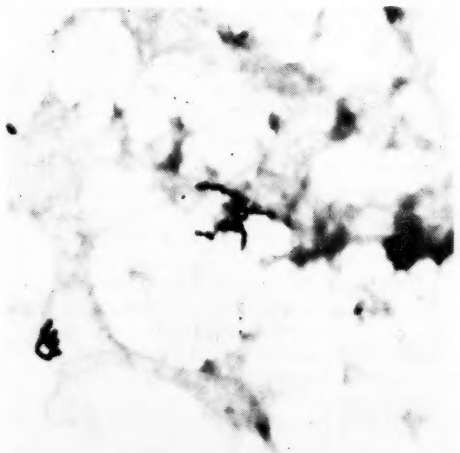

Fig. 2—Preparation of gallstone showing actinomyces. (Gram's stain.)

were recorded of the colouring (table I) and the number of layers (table II). The greater proportion of stones showed either 2 or 3 layers, while 8 stones only were apparently homogenous in constitution. 4 or more distinct layers were found in 6 stones. If clearly defined layering was seen, samples for analysis were carefully taken from each layer, avoiding contamination with material from adjacent layers. If the stone appeared to be homogenous in composition, a small amount was ground to a fine powder for analysis.

The micromethods described by Holt and Tarnoky (1953) were used, tests being performed for the detection of protein, cholesterol, bile-pigments, calcium, phosphorus, iron, and carbonate. In tables III and IV the positive results (whether as a " trace ", " positive ", or " strongly positive ") are expressed simply as indicating the presence of the substances in the stone. Table III gives the results of analysis of the whole stone and table IV the findings in the central layer—or " nucleus ". Homogeneous stones are included in table IV as well as table III. The results of culture showing the presence of actinomyces are included in each table.

TABLE I—ANALYSIS OF 57 STONES

No. in series	Colour and no. of stones	Direct smear	Cultures		Serology (actinomyces)			
			Aerobic bacteria	Actinomyces	Slide agglutination	Tube agglutination	Absorbed sera* cult. 4 (hom.)	Absorbed sera* cult. 43
1	Brown, dark yellow, white (1)	–	*E. coli*	Absent	..	..	..	..
2	Yellow (389)	–	Absent	Present (19 days)	+	1 in 25	–	–
3	Yellow, white, green (2)	–	Absent	Present (16 days)	+	1 in 50	–	–
4	Grey-brown (3)	–	*E. coli*	Present (16 days)	+	1 in 25	–	–
5	Dark grey and yellow (15)	–	Sterile	Sterile	..	..	..	..
6	Grey (1)	–	Absent	Present (17 days)	+	1 in 25	–	–
7	Dark brown and grey (40)	–	Absent	Present (17 days)	+	1 in 25	–	–
8	Brown (21)	–	*B. neapolitanum*	Present (18 days)	+	1 in 50	–	–
9	White, grey, brown (1)	–	Absent	Present (14 days)	+	1 in 50	–	–
10	Light brown (14)	–	Absent	Present (12 days)	+	1 in 50	–	–
11	Grey-white (7)	Gram-+ve rods showing branching. Tight clusters	*Staph. albus*	Present (12 days)	+	1 in 50	–	–
12	White, grey, brown (1)	–	Absent	Present (10 days)	+	1 in 25	–	–
13	Yellow (81)	–	Sterile	Sterile	..	..	..	..
14	Cream, rust (25)	–	Sterile	Sterile	..	..	..	..
15	Black (1)	–	Sterile	Sterile	..	..	..	..
16	Pale cream (4)	–	Gram-+ve rods slender and slightly beaded, showing very scanty branching. Grows aerobically and anaerobically. Colony, moist flat entire edge. ? corynebacterium		..	..	..	..
17	Deep red (4)	–	*E. coli*	Absent	..	..	..	..
18	Black. Gravel	–	*B. acidi lactici*	Absent	..	..	..	..
19	Pale yellow. Gravel	–	*B. acidi lactici*	Present (19 days)	+	1 in 50	–	–
20	Grey (8)	–	Sterile	Sterile	..	..	..	..
21	Rust (3)	–	Sterile	Sterile	..	..	..	..
22	Pale brown (1)	–	Sterile	Sterile	..	..	..	..
23	Dark red (2)	–	*Staph. pyogenes*	Absent	..	..	..	..
24	Buff (6)	–	Sterile	Sterile	..	..	..	..
25	Pale green and off-white (2)	–	Absent	Present (32 days)	+	1 in 50	–	–
26	Dark green (2)	–	Contaminated. Gram-+ve sporing *B. subtilis* type		..	..	..	..
27	Cream and green (1)	–	*Staph. pyogenes*	Present (16 days)	+	1 in 25	–	–
28	Black (2)	Doubtful gram-+ve rods or cocci. Beaded. Very scanty	*Staph. albus*	Present (14 days)	+	1 in 50	–	–
29	Pale brown (1)	Very scanty gram-+ve rods	*Staph. albus*	Absent	..	..	..	..
30	Yellowish cream (1)	–	Sterile	Sterile	..	..	..	..
31	Deep yellow (139)	–	Absent	Present (27 days)	+	1 in 50	–	–
32	Deep brown (17)	–	Sterile	Sterile	..	..	..	..
33	Pale brown (2)	–	Absent	Present (22 days)	+	1 in 50	–	–
34	Dark grey (15)	–	Absent	Present (27 days)	+	1 in 125	–	–
35	Brown (2)	–	Sterile	Sterile	..	..	..	..
36	Off-white (7)	–	Contaminated with spore-forming rod of the subtilis type		..	..	..	..
37	Reddish-brown (25)	–	*Staph. albus*	Absent	..	..	..	..
38	Buff (9)	Very scanty gram-+ve cocco-bacilli	Absent	Present (87 days)	+	1 in 50	–	–
39	Cream (1053)	–	Contaminated with spore-forming bacillus		..	..	..	..
40	Light brown and black (216)	–	*Staph. albus*	Absent	..	..	..	..
41	Grey (11)	–	*Staph. albus*	Absent	..	..	..	..
42	Brown (1)	–	Sterile	Sterile	..	..	..	..
43	Pale cream (1)	–	Absent	Present (27 days)	+	1 in 50	–	–
44	Pale brown (2)	–	*B. coscoroba* (*E. coli* immobile)	Present (27 days)	+	1 in 50	–	–
45	Dark grey (1)	–	Sterile	Sterile	..	..	..	..
46	Light brown and black (1227)	–	Absent	Present (46 days)	+	1 in 50	–	–
47	Dark grey (5)	–	Absent	Present (57 days)	+	1 in 25	–	–
48	Brown (2)	–	*Aerobacter aerogenes, B. neapolitanum, Streptococcus fæcalis*	Present (25 days)	+	1 in 25	–	–
49	Dark grey (4)	–	Sterile	Sterile	..	..	..	..
50	Black (1)	–	Absent	Present (42 days)	+	1 in 50	–	–
51	Black (1)	–	Contaminated spore-forming bacillus. *B. subtilis type*		..	..	..	..
52	Pale blue (2)	–	Absent	Present (43 days)	+	1 in 50	–	–
53	Black (1)	–	Absent	Present (42 days)	+	1 in 50	–	–
54	Pale brown and black (6)	–	Hæmolytic streptococcus	Present (42 days)	+	1 in 125	–	–
55	Light brown (3)	–	Absent	Present (21 days)	+	1 in 25	–	–
56	Dark brown. Gallbladder and stones	Few gram-+ve cocco-bacillary forms	Absent	Present (46 days)	+	1 in 50	–	–
57	White (1)	–	Absent	Present (19 days)	+	1 in 50	–	–

* Negative result indicates presence of species with similar characteristics and absence of another species.

TABLE II—NUMBER OF LAYERS IN 57 SPECIMENS OF GALLSTONES AND PRESENCE OF ACTINOMYCES (CULTURE) IN EACH TYPE OF STONE

No. of layers	No. of stones	Actino. positive (%)
Homogeneous	8	3 (*37·5*)
2	22	9 (*41*)
3	21	12 (*57*)
4+	6	6 (*100*)
Total	57	30 (*52·6*)

Though the number of gallstones containing four or more layers is small, it seems that as the number of layers increase, so do the chances of isolating actinomyces.

Commentary on Chemical and Bacteriological Findings

Chemistry

Analysis of the whole stone (table III) and the centre of the stone (table IV) confirmed the presence of recognised constituents of gallstones. It also showed that no one constituent, particularly cholestrol and bile-pigment, is dominant. Rovsing's theory—that bile-pigment is at the centre of every gallstone—did not seem to be upheld by the analysis. But 8 stones in which pigment was not detected by Foucet's test did show a macroscopic discolouration of the centre. The nature of this residual pigment has still to be defined. It may correspond to that similar residual pigment named bilihumin by earlier investigators (Städeler, cited by Hammarsten 1914).

TABLE III—OVERALL ANALYSIS OF 57 SPECIMENS OF GALLSTONES AND ANALYSIS OF 30 STONES CONTAINING ACTINOMYCES

Substance	Analysis of 57 stones (%)	Analysis of 30 actino-stones (%)
Protein	49 (*86*)	25 (*83*)
Cholesterol	47 (*82*)	22 (*73*)
Bile-pigment ..	45 (*79*)	25 (*83*)
Carbonate	46 (*81*)	24 (*80*)
Calcium	20 (*35*)	13 (*43*)
Phosphorus	14 (*25*)	6 (*20*)
Iron	7 (*12*)	3 (*10*)

The analysis is of special interest in showing that protein and carbonate merit as much study as cholesterol and bile-pigment. Mårtensson (1941) also drew attention to the presence of protein and cites Lichtwitz as showing that cholesterol can be precipitated by albumen. In view of recent interest in the phenomenon of chelation in relation to the initiation and growth of calculi (Boyce et al. 1955), the protein may bear a special relationship to the calcium present. Yet the results of this analysis show that the occurrence of calcium does not correspond with that of protein, and neither with bile-pigment nor even carbonate, though conjugation with any of these is to be expected. Carnot and Gruzewska (1928) declared the presence of an abnormal protein, cholenuclein, in the bile of cholecystitis and cholelithiasis. This was said to be related to organ nucleoproteins and was possibly the result of epithelial cell destruction.

Bacteriology

Rosenow (1914) examined the centre of 30 gallstones. In 25, streptococci were isolated; in 5, *E. coli*; in 1, *B. typhosus*; in 2, *E. coli* and *B. welchii*. Illingworth (1927) examined 23 stones, finding 7 infected (2 with streptococci, 3 with *E. coli*, and 2 with staphylococci). Rosenow and Illingworth had, in addition, examined the walls of 29 and 100 gallbladders respectively. Rosenow isolated streptococci in 21 and *E. coli* in 10. Illingworth found streptococci in 34, *E. coli* in 3, and staphylococci in 2. It is difficult to postulate why, in that period of years, the streptococcus was the organism to be isolated by these and several investigators; why, in the last decade of the nineteenth century *B. typhosus* and *E. coli* were often isolated. According to Cushing, Flexner found typhoid in 50% of cases of cholecystitis, and Gilbert and Fournier had even classified biliary lithiasis into two groups: lithiasis due to *E. coli* and lithiasis due to *B. typhosus*. Perhaps the variance in the bacteriological findings is a reflection of the changes in disease incidence over the passage of time; typhoid fever was declining in incidence at the beginning of this century but diseases attributable to the streptococcus were prevalent up to the chemotherapeutic era.

TABLE IV—ANALYSIS OF CENTRE OF 57 SPECIMENS OF GALLSTONES (HOMOGENEOUS STONES INCLUDED), AND ANALYSIS OF 30 STONES CONTAINING ACTINOMYCES

Substance	Analysis of 57 stones (%)	Analysis of 30 actino-stones (%)
Protein	37 (*65*)	18 (*60*)
Cholesterol	43 (*75*)	20 (*66*)
Bile pigment ..	42 (*74*)	23 (*76*)
Carbonate	33 (*58*)	15 (*50*)
Calcium	14 (*25*)	10 (*33*)
Phosphorus	11 (*20*)	6 (*20*)
Iron	5 (*10*)	2 (*6*)

Of the 57 stones examined in this series, *E. coli* were found in 4, a streptococcus in 2, and a staphylococcus in 8. But the finding of actinomyces in 30 stones was quite unexpected. Further, the serological tests indicate this species is not the actinomyces of Wolff and Israël.

A further, though complex, extension of such an investigation would therefore be concerned with the old theory of blood-borne spread from a focus of infection, and such a source could be the mouth. Martensson cites Naeslund (1925) among others as bringing actinomyces into prominence with regard to pathology of salivary and dental calculus, and he discusses the role such an organism may play in producing the calcified stone of such concretions and scales.

Correlation Between Chemical and Bacteriological Findings

Naeslund considered that the mycete caused the precipitation of calcium salts in a colloid solution. Citron (1945), in this context, demonstrated the alkaline phosphatase activity of the *Actinomyces israëli* and showed that the precipitation of calcium only occurs in a solution which contains organic phosphate. Certainly, dental tartar and salivary calculi contain a large amount of calcium phosphate (76%) (Glock and Murray 1938). Tables III and IV show that in this investigation there is no significant difference between those stones or stone centres which contained actinomyces and those which did not. Unlike salivary calculi, carbonate and not phosphate is dominant in gallstones. Thus any further eludication of this problem will involve further analyses, bacteriological, chemical, and extensive serological techniques.

Summary

The early theories, chemical and bacteriological, of the cause of gallstone formation are outlined. Research into the reproducibility of previous findings, as part of a wider programme of investigations, led to a study of whole and central portions of 57 specimens of gallstones by qualitative chemical analysis and the bacteriological methods of direct smear, culture and serology.

An actinomyces was isolated from 30 of the 57 specimens. The serological character of each organism indicates the presence of a species distinct from *Actinomyces bovis*. The findings of previous investigators were not confirmed and a possible explanation is given.

Chemical analysis did not confirm any dominance of cholesterol or bile-pigment especially in the centre of the

stones and shows that protein and carbonate deserve as much attention. There is no apparent difference in the stones that did and did not grow actinomyces.

The old theory of blood-borne infection causing a gall-bladder lesion and calculus formation from a distant focus, such as the mouth, is reintroduced with reference to a species of actinomyces found in oral concrements.

An indication is given of the uses of serology and bacteriological chemistry (with respect to protein and inorganic constituents) in the furtherance of such research.

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INOPERABLE CANCER OF THE BRONCHUS TREATED BY MEGAVOLTAGE X-RAY THERAPY

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IN a previous article (Morrison and Deeley 1957) we gave a preliminary report of the results of treatment of inoperable carcinoma of the bronchus by megavoltage X-ray therapy. We described the palliative benefits, and gave the one-year survival-rate in a group of 199 patients. We now report the later progress of the same group, with an additional 78 patients treated since 1957.

The Patients

All the patients treated had a carcinoma of the bronchus, which was considered inoperable either because of advanced local disease or because the respiratory reserve was insufficient to allow lung resection to be performed. We considered these patients were suitable for a course of radiotherapy aimed at curing the disease, because they were still in reasonably good general health, with no clinical evidence that the disease had spread outside the chest. Patients who had had a previous operation on the chest, apart from an exploratory thoracotomy, were excluded from the series. Of the 277 patients who completed a radical course of treatment, 257 (93%) were men and 20 (7%) were women.

Attempts were made to obtain histological proof of the diagnosis either by biopsy at the time of bronchoscopy or, in peripheral tumours, by drill biopsy through the chest wall. In 7 patients the clinical diagnosis was confirmed by isolation of malignant cells from the sputum. In 48 patients (17%) histological confirmation was not obtained, the diagnosis of carcinoma being based on the clinical and radiological findings.

The histological types of the 277 tumours treated were:

Squamous	135 (49%)
Anaplastic and oat-celled	78 (28%)
Adenocarcinoma	8 (3%)
Malignant cells in sputum	7 (3%)
Carcinoma of unspecified type	1
No histology or negative histology	48 (17%)

The main site of involvement of the primary tumours is shown in table I. 1 patient had bilateral lesions involving the right middle lobe and left upper lobe; we regarded these

TABLE I—SITE OF THE PRIMARY TUMOURS

Left			Right				Bilateral lesions
Main bronchus	Upper lobe	Lower lobe	Main bronchus	Upper lobe	Lower lobe	Middle lobe	
35 (12·7%)	66 (23·9%)	44 (15·9%)	29 (10·4%)	64 (23·2%)	34 (12·3%)	4 (1·4%)	1
Total = 145 (52%)			Total = 131 (48%)				1

as separate primary tumours and each received radical treatment.

We attempted to divide the cases into two groups: patients with and patients without evidence of lymph-node involvement of the mediastinum. The evidence for mediastinal-node involvement was based on the clinical, radiological, bronchoscopic, or thoracotomy findings. Table II gives the incidence of involvement, and shows that anaplastic tumours have a higher rate of node involvement than squamous-cell tumours. A similar finding was reported by Hinson (1958).

Treatment

The treatment was given by an 8-million-volt linear accelerator installed by the Medical Research Council at Hammersmith Hospital. The physical characteristics of the X-ray beam produced by this machine, and the clinical advantage of megavolt compared with 240 kV radiation have been discussed (Morrison, Newbery, and Deeley 1956). The greater energy of megavolt X-rays enables the tumour to be given higher doses of radiation with fewer harmful effects to the skin and subcutaneous tissues, and with a lower total-body dose. Hence, both the local and general radiation reactions after megavoltage therapy are less than after 240 kV therapy.

The treatment was planned to give a mean dose to the tumour of 4500 rad units in four weeks by daily exposures. When a very large field had to be used, and a greater total volume of tissue was irradiated, the dose was reduced to 3600 rads. Nearly all the patients were able to tolerate the whole course, and few had any of the disturbing reactions often associated with radiation therapy.

The region irradiated included the area of tumour opacity, as seen in posteroanterior and lateral radiographs, with a zone

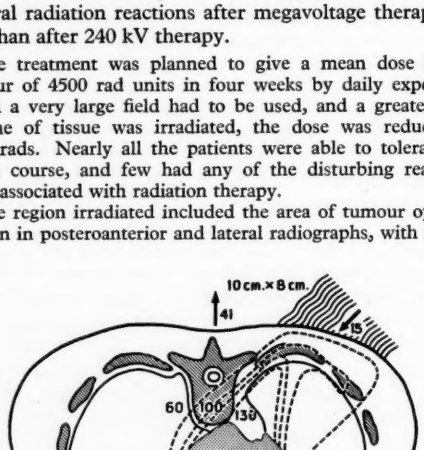

Fig. 1—Cross-section of chest, showing position of fields and distribution of radiation.

TABLE II—THE EXTENT OF THE PRIMARY TUMOUR IN THE TWO MAIN HISTOLOGICAL TYPES

—	Squamous	Anaplastic
No mediastinal involvement	57 (*42%*)	24 (*31%*)
Evidence of mediastinal involvement ..	78 (*58%*)	54 (*69%*)
Total	135	78

of 2 cm. of apparently normal lung surrounding the opacity and the mediastinal-node areas. Because of the sharp definition of the beam, it was possible to avoid irradiating the spinal cord and to spare the opposite lung as much as possible by a simple arrangement of two fields (fig. 1).

Before starting the radiotherapy most of the patients were admitted to hospital for treatment to improve their general health, and to treat any associated infection in the lung.

Results

The *relief of symptoms* by this treatment has been discussed in our previous article. Hæmoptysis was arrested in 94% of cases, and about 75% of patients with dyspnœa, pain, or cough were also relieved. The palliation did not differ in the squamous and anaplastic types of growth.

The *survival-rates* have been calculated by the life-table method. Fig. 2 shows the yearly survival for all the patients for five years after treatment, and it will be seen that 6% lived for five years or more. After three years the risk of dying from the disease is small, and a three-year

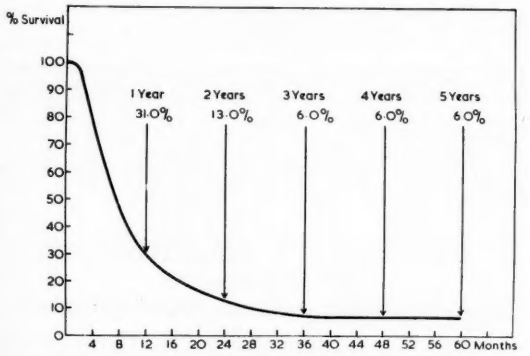

Fig. 2—Survival curve after treatment of carcinoma of the bronchus.

survival-rate seems to give a satisfactory index of the value of the treatment in curing or controlling this disease.

In table III the results are analysed according to the histological findings. In squamous-cell tumours the three-year survival-rate was 8·9%, but only 1 patient (1·5%) with an anaplastic-cell tumour survived for three years. This table also shows that the chance of survival is best (10%) in squamous-cell tumours with no evidence of mediastinal spread.

The cases were divided into three groups according to whether the tumour arose in the main bronchus, the upper-lobe (including the middle-lobe) bronchus, or the lower-lobe bronchus. As there was no significant difference in the distribution of the histological types or in the incidence of mediastinal spread at the three sites, it was possible to compare the effect of the site of origin on the survival-rate. Table IV shows that the prognosis is significantly better for patients with upper-lobe (and middle-lobe) tumours than for patients with lower-lobe tumours. The same difference in the survival-rates between tumours of the upper and lower lobes was found in patients treated with 240 kV X rays (Brown 1952), and in those who had a resection (Carlisle et al. 1951, Bignall and Moon 1955).

Other Reported Results

The survival-rates which have been reported in inoperable carcinoma of the bronchus up to five years after treatment by radiotherapy are shown in table V. These range from 2% to 10% at three years. One cannot compare these results or the techniques employed without knowing the method of selection of the patients for treatment, the distribution of the histological types, and other factors known to affect prognosis.

TABLE III—RELATION OF HISTOLOGICAL FINDINGS, MEDIASTINAL SPREAD, AND SURVIVAL-RATES

—	Squamous			Anaplastic		
Spread	All cases	Without mediastinal spread	With mediastinal spread	All cases	Without mediastinal spread	With mediastinal spread
3-year survival	8·9%	10%	7%	1·5%	0%	2%

TABLE IV—EFFECTS OF THE SITE OF THE PRIMARY TUMOUR ON THE 3-YEAR SURVIVAL-RATE

—	Main bronchus	Upper and middle lobes	Lower lobe
No. of cases	63	134	80
3-year survival ..	5%	9%*	2%*

* The difference between these results is statistically significant.

Comparison with Patients Treated with 240 kV X Rays

As we mentioned in our previous article, very few patients having megavoltage therapy suffer from the constitutional effects of the radiation, and the only troublesome local effect is mild dysphagia in a small proportion of them. Because of the diminished reactions, larger tumours can be treated with megavoltage therapy than with conventional deep X-ray therapy, and megavoltage radiation can therefore be used in the treatment of patients who formerly would have been unsuitable for radical treatment.

In a group of 176 patients treated with 240 kV therapy at this hospital between 1949 and 1953, the three-year survival-rate was 2%.

Table VI shows the survival-rates for 240 kV therapy compared with 8-million-volt therapy in the squamous and anaplastic tumours. Although more advanced cases were included in the group treated at the higher energy, the survival-rates are slightly better for squamous-cell

TABLE V—RECENT REPORTS OF SURVIVAL-RATES AFTER RADICAL-RADIATION TREATMENT

Report	No. of cases	Energy of radiation	Tumour dose	% proved	% survival (yr.)				
					1	2	3	4	5
Hilton and Pilcher (1955)	203	..	4000–5500r	63	27	11	..	..	4
Schulz (1957) ..	385	250 Kv	4000r	..	15	5	3	1	1
Smithers (1955) ..	171	240 kV	5000–7000r	60	37	13	9	6	4
Krabbenhoft and Leucutia (1958)	132	2 MeV and 250 kV	Various	100	12	8	..	..	2
Shanks (1959) ..	136	240 kV	4000r	..	31	15	10	3	2
Hammersmith Hospital (1949–53)	176	240 kV	3250–4000r	61	24	11	2	1	1
Present series (1953–58)	277	8 MeV	4500 rads	83	30	14	6	5	6

TABLE VI—COMPARISON OF SURVIVAL-RATES AFTER 8-MeV AND 240-kV X RAYS

—	Squamous		Anaplastic	
Therapy ..	8 MeV	240 kV	8 MeV	240 kV
No. of cases ..	138	68	78	45
Survival:				
1 year ..	38·0%	24·2%	15·2%	15·5%
2 „ ..	18·4%	16·5%	6·0%	6·6%
3 „ ..	8·9%	4·5%	1·5%	0%

lesions. The results of treatment for the two methods differ little in the anaplastic-cell tumours.

Indications for Radical Treatment

As a result of treating this series we have formed an idea of the type of patient likely to benefit from radical megavoltage therapy. We now consider that this is indicated in patients with inoperable disease who are not severely debilitated, who have no evidence of spread outside the chest, and who have the squamous-cell type of tumour. When the lesion is of the anaplastic or oat-cell type the chance of survival is very poor, and there seems to be less justification for subjecting the patient to a long course of radiation therapy. Short courses of treatment, however, may be given to relieve distressing symptoms. In patients with chronic bronchitis, or other chronic inflammatory disease, the radiation reactions are more severe than in lungs unaffected by previous disease, and it is often impossible to give a sufficient dose of radiation to eradicate the growth. The radiation may also aggravate the cough and increase the quantity of sputum.

A serous pleural effusion does not always indicate pleural involvement by growth, but an effusion which contains blood or malignant cells suggests a widespread intrapleural dissemination which cannot be adequately treated.

Discussion

Failure to cure carcinoma of the bronchus can be attributed to incomplete response of the primary growth to the radiation, or to early dissemination of tumour cells outside the treated area. At the time of treatment some patients may already have distant metastases which cannot be detected clinically. A number of tumours, however, do not disseminate widely, and even at death are still confined to the chest.

The extent of the disease, macroscopically, in 31 cases at postmortem was:

	Anaplastic	*Squamous*
No. of cases	11	20
Spread outside chest	7 (*63%*)	7 (*35%*)
No spread outside chest	4 (*37%*)	13 (*65%*)

In 176 patients who were examined regularly after treatment until the time of death, a similar proportion showed no sign of spread:

	Anaplastic	*Squamous*
No. of cases	71	105
Clinical signs of disease outside the chest ..	52 (*73%*)	34 (*32%*)
No signs of disease outside the chest ..	19 (*27%*)	71 (*68%*)

These findings represent the extent of the disease terminally; but, if one assumes that any dissemination which becomes evident later will already have occurred at the time of treatment, there are roughly 2 out of 3 patients with squamous lesions, and 1 out of 3 patients with anaplastic lesions in whom the tumour is apparently still confined to the primary site and who are potentially curable. In about half the patients treated, therefore, the disease could probably be cured by effective local treatment.

The dose of radiation which may be given to any tumour is limited by the tolerance of the surrounding normal tissues, and in the majority of cases this dose appears to be insufficient to destroy the tumour completely. With high-energy radiation, a relatively greater tumour-to-normal-tissue dose ratio is possible than with 240 kV X rays, permitting a slightly higher tumour dose to be given with less damage to the normal tissues. With a further increase of radiation energy, however, it seems unlikely that this ratio will increase any further.

Summary

277 patients with inoperable carcinoma of the bronchus have received radical treatment with megavoltage X rays. The results of treatment and the survival rates are given.

With megavoltage therapy there are fewer systemic and local radiation reactions, making it possible to treat larger and more extensive tumours.

The chances of survival are greater with squamous-cell tumours (three-year-survival-rate 8·9%) than with anaplastic-cell tumours (three-year-survival-rate 1·5%).

Radical X-ray treatment of carcinoma of the bronchus (squamous-cell type) is indicated when the tumour is inoperable in patients who are not severely debilitated, and who have no evidence of spread outside the chest.

Local X-ray treatment may fail because the primary growth responds incompletely, or because of early dissemination of tumour cells.

We should like to thank Dr. C. A. P. Wood, director of the M.R.C. Radiotherapeutic Research Unit, Dr. L. H. Walter, and Dr. P. B. Woodyatt for referring their patients to us for treatment.

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ACQUISITION OF STAPHYLOCOCCI BY NEWBORNS

DIRECT VERSUS INDIRECT TRANSMISSION *

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PATHOGENIC staphylococci acquired by newborn infants in hospital nurseries are responsible for a high incidence of minor diseases, such as impetigo and conjunctivitis, and a significant rate of more serious illnesses, such as mastitis, septicæmia and pneumonia, which arise some

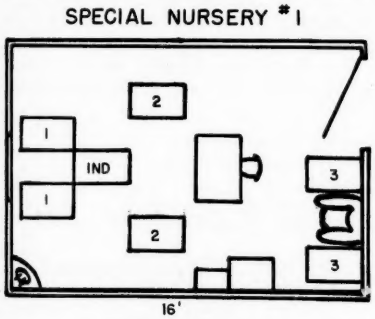
* These studies were sponsored by the Commission on Streptococcal Diseases of the Armed Forces Epidemiologic Board, and supported by the Office of the Surgeon General, Department of the Army, Washington, D.C.

months after discharge from hospital both in the infants and in members of their families. The rates of acquisition of these staphylococci by newborn infants vary from time to time, but, during periods of widespread dissemination of the organism to the infants, epidemics of staphylococcal disease are common. Such epidemics are ordinarily well established by the time they are recognised, because the clinical manifestations usually do not appear until after the infants have been discharged from the hospital. Interruption of the epidemics is attempted by identification and removal of all possible human and environmental sources of the offending organism—a procedure requiring complex and extensive bacteriological surveys and techniques—or by continuous prophylactic administration of antibiotics to all infants. The development of more rational methods to interrupt the spread of the organisms to the infants is hampered by paucity of information concerning modes of transmission of staphylococci.

The nurseries at this hospital have been the sites of endemic and intermittently epidemic staphylococcal disease for several years. The usual methods of control have resulted in only temporary amelioration. The present study represents a preliminary effort to define the important modes of transmission so that methods for control of these infections may be developed. The study was designed primarily to determine whether infant-to-infant spread was direct (heavy droplets projected short distances) or indirect (airborne droplet nuclei or dust).

Method

A small room, 11 by 16 ft., was employed as a special nursery (see figure). Circulation of air was maintained by a fan. An "index" infant, known to be a nasal carrier of a bacteriophage-typable strain of staphylococci, was placed in a bassinet at one end of the room. Newborn infants were admitted directly from the delivery room to 1 of 6 bassinets set at fixed distances from the index baby, and were retained in these bassinets without removal for forty-eight hours. 2 of these bassinets (position 1) were placed immediately adjacent to the index baby, 2 (position 2) at a distance of 4½ ft., and 2 (position 3) at 11 ft. The 6 infants were cared for by a staff of the same three nurses working in eight-hour shifts. These nurses wore masks which were changed frequently. On entering the nursery they scrubbed their hands and arms for three minutes with 'Phisohex' and washed with the same preparation between contacts with different infants. The index baby was observed but not touched by these nurses and administered to only when necessary by outside personnel summoned by the special nurse. All other persons were excluded. After forty-eight hours of exposure to the index baby, each infant was removed to the main nursery and another study infant was admitted. A different index infant was employed each week. It was anticipated that, if airborne droplet nuclei had a major role in transmission, organisms should be acquired at random in all bed positions. Organisms spread directly by heavy droplets should appear predominantly in infants located near the index baby.



Plan of study nursery.

Cultures of the anterior nares of each study infant were procured twice daily for four days (including the forty-eight hours in the special nursery) and daily thereafter until discharge, usually on the fourth day. Cultures were obtained from 57% of the infants three to six weeks after discharge. The anterior nares of all involved personnel were cultured twice weekly. Swabs were inoculated on to mannitol agar plates containing 7% salt, which were incubated at 37°C for forty-eight hours. Two to four mannitol-fermenting colonies were picked from each positive plate for bacteriophage typing. An infant was considered to have acquired an organism if it was recovered repeatedly or if it appeared in profusion on the final culture.

Findings

48 infants were exposed to index babies carrying strains of staphylococci whose bacteriophage-typing characteristics were clearcut and reproducible (types 80/81 and 3B/3C/71). An organism identical to that of the index baby was acquired by only 1 infant; he was in a bassinet immediately adjacent to the index infant. 43 babies were exposed to index infants carrying strains whose bacteriophage-typing characteristics were somewhat variable (7/47/53/54/75). 7 of these babies acquired organisms whose typing patterns were similar, but not identical, to those of the index baby's strain. The source of these organisms could not be determined with certainty. Two of these strains differed only slightly, and therefore were probably the same as that of the index infant; both of these infants were located in bassinets at position 1. The patterns of five other strains were less similar but nonetheless impossible to differentiate from the index strain, and accordingly were considered to be possibly the same. 1 infant was at bassinet position 1, and 2 each at positions 2 and 3.

In contrast to the relatively low rate of spread from infant to infant, there was a high rate of acquisition of organisms of bacteriophage types identical to those carried by two of the three special nurses. (The third nurse exhibited repeatedly negative cultures.) 21 of 95 infants acquired a strain carried by nurse A (80/81/52/52A), and 12 babies acquired the strain of nurse B (3A/3B/3C). When it became apparent that the infants were being infected predominantly by the organisms carried by the nurses and not those of the index babies, nurse A was relieved of all active duties during the fifth and sixth weeks of the study, but she was required to spend each of her eight-hour shifts unmasked and seated in a chair between (and immediately adjacent to) 2 study bassinets. She resumed her full duties wearing a mask during the final two-week period of the study. The accompanying table shows that nurse A's organisms failed to appear in any infants who were exposed to her during the fifth and sixth weeks of the study, but her strain again reappeared during the final two weeks. Nurse B worked overtime in the nursery to accomplish nurse A's duties during the two weeks that nurse A sat in the chair; it was at this time that her type appeared more frequently in the exposed infants.

ACQUISITIONS OF STAPHYLOCOCCAL STRAINS CARRIED BY NURSES

Weeks of study	Infants		
	No. exposed	Acquisitions	
		Nurse-A type	Nurse-B type
1–2	24	11	1
3–4	23	4	0
5–6	24	0*	7
7–8	24	6	4
Totals	95	21	12

* During weeks 5–6 nurse A sat in room, unmasked, without touching infants.

The results of this study suggested that personnel-to-infant spread of staphylococci was of relatively greater importance than infant-to-infant airborne spread, and that handling of the infants was required for such personnel-to-infant transmission. A subsequent study has confirmed that spread of a carrier's organism to newborn infants does occur by handling alone. In this study infants were admitted to an ' Isolette ' incubator directly from the delivery room. This incubator is a closed, heated unit to which outside air is pumped via a hose from an outside window. Access to the infant is afforded by portholes which permit entry of the hands and forearms of the nurse. Thus spread of organisms from personnel to infant is unlikely except by hand-to-infant transmission.

37 infants were placed in the incubator shortly after birth by personnel known to be free of staphylococci. One of 3 " index " nurses then administered " initial care ", consisting of washing the infant with cotton balls and water, taking the rectal temperature, combing the infant's hair, and dressing the infant. The hands of the nurses were not washed immediately before handling the infant. Each of these index nurses carried in the anterior nares a different bacteriophage type of staphylococci (80/81, 80/81/52/52A, and 3A/3B/3C). Each infant was exposed on this one occasion and was then placed in the main nursery, where there were no personnel carrying staphylococci of types similar to those of the index nurses. 20 (54%) of the 37 infants acquired the strain of the appropriate nurse after this sole exposure, as determined by umbilical and nasal cultures.

Conclusion

The results of these studies indicate that personnel-to-infant spread of organisms has a major role in the dissemination of staphylococci in nurseries for the newborn, and that this spread is predominantly from the hands of the carrier to the infant. Spread from infant to infant by the airborne route appears to be of lesser importance. Further studies of means by which this dissemination from personnel to infant may be interrupted are in progress.

This study was made possible by the complete cooperation of the department of nursing and especially of Miss Phyllis Fischer, R.N., Miss Dorfetta Griffin, R.N., Mrs. Norma Jenkins, R.N., and Mrs. Shirley Hill, P.N. We thank Mrs. Norma Brunk for technical assistance.

EFFECT OF THE SULPHONYLUREAS ON FIBRINOLYSIS

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IN the study and treatment of thromboembolic disease much attention has been paid to the obverse side of the coin, coagulation; the reverse side, fibrinolysis, may be equally important. There are two possible approaches to the use of fibrinolysis as a therapeutic agent. First we might activate plasminogen, by the intravascular injection of either streptokinase or the " activator " which is thought to be produced when serum is treated with streptokinase. This is being extensively tried in the U.S.A. Secondly we might enhance the natural fibrinolytic mechanism pharmacologically (Fearnley 1960).

A biphasic response of blood fibrinolytic activity to a single injection of insulin has been reported in diabetes, consisting of an initial reduction in parallel with blood-glucose levels, followed by a rebound increase at low blood-glucose levels (Fearnley, Vincent, and Chakrabarti 1959). This suggested that the sulphonylurea compounds, by lowering blood-glucose levels, might increase blood-fibrinolytic activity in non-diabetic subjects. The conjecture has proved correct, but the observed increase of fibrinolytic activity is not directly related to hypoglycæmia; some other mechanism may be responsible. We here report the effect of tolbutamide or chlorpropamide in eight arteriosclerotic inpatients.

Patients and Methods

The patients were one woman and seven men suffering with arteriosclerotic disease of the heart or limbs; two had status anginosus, and six had intermittent claudication. Fasting blood was obtained daily (except Sundays) before the patient got up, at 8 A.M. $\pm$15 minutes, for measurement of blood fibrinolytic activity and blood-glucose. After a control period of 4–6 days the patients were given either tolbutamide or chlorpropamide in the doses stated; the former was given in divided doses and the latter as a single dose at 9 P.M.

The fibrinolytic activity of the blood was measured by the method of Fearnley et al. (1957). The results are expressed as lysis-times in hours, and are the means to the nearest half-hour of duplicate determinations. Readings were not made beyond 24 hours, so that all lysis-times of greater duration are expressed as 24 hours. When necessary the photographic modification of Lackner and Goosen (1959) was employed. As blood-fibrinolytic activity and lysis-time are inversely related, a decrease of lysis-time signifies an increase of fibrinolytic activity and vice versa. Blood-glucose was measured by the method of Folin and Wu, the blood samples being collected in fluoride tubes and the determinations made within 3 hours of collection.

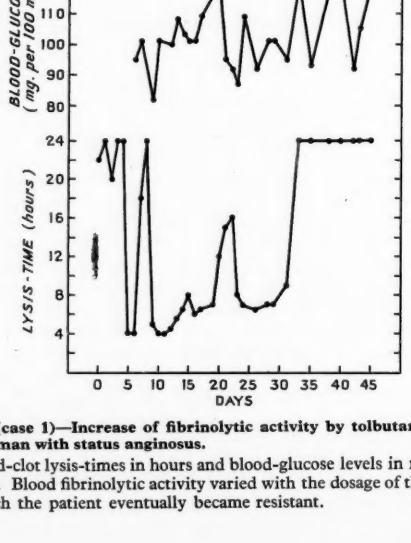

Fig. 1 (case 1)—Increase of fibrinolytic activity by tolbutamide in a woman with status anginosus.

Blood-clot lysis-times in hours and blood-glucose levels in mg. per 100 ml. Blood fibrinolytic activity varied with the dosage of the drug to which the patient eventually became resistant.

Serum-cholesterol was measured at intervals, but as no significant change took place the figures are not given.

Results of Treatment

Case 1 (fig. 1).—Woman, aged 69. Effort angina for 4 years. Admitted with acute coronary insufficiency and treated for 3 weeks with anticoagulants. Severe pain at rest and on slight exertion kept her confined to bed, and 3 months after admission she was given tolbutamide. Mean control lysis-time, 22·8 hours. Tolbutamide 500 mg. t.d.s. was followed within 24 hours by a reduction of lysis-time to 4 hours. The drug was stopped after 48 hours, and the lysis-time increased to 18 and 24 hours. Tolbutamide 500 mg. t.d.s. was then re-started, and again the lysis-time fell to 5 hours. Fig. 1 shows that the lysis-time reflected alterations of dosage, and that she eventually became resistant, the lysis-time reverting to 24 hours. Within a few days of receiving tolbutamide the severity of her pain diminished, and within 2 weeks she was free from pain at rest. She remained free of pain for a further 6 weeks when another attack of acute coronary insufficiency was followed by congestive failure from which she died.

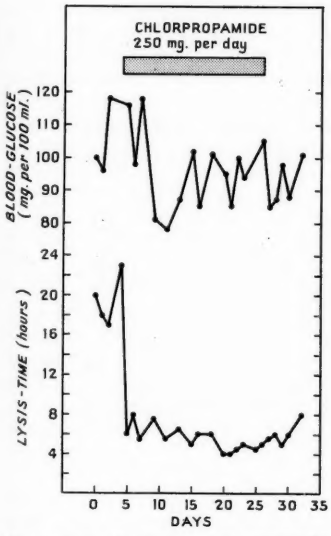

Fig. 2 (case 3)—Increase of fibrinolytic activity by chlorpropamide in a man with status anginosus.

Case 2.—Man, aged 57. Intermittent claudication of left leg for 2 years, worsening recently. Right leg similarly affected for a month. Pain after walking 15-20 yards. Pulsation absent in left dorsalis pedis and posterior tibial arteries. Mean control lysis-time, 5·4 hours. On tolbutamide 500 mg. t.d.s., the lysis-time was reduced to 2·5 hours and during the next 20 days varied between 2·5 and 3·5 hours. The patient was discharged on tolbutamide 500 mg. t.d.s., and when last seen 2 months after discharge from hospital, could walk 1–2 miles without pain.

Case 3 (fig. 2).—Man, aged 55. Status anginosus for 4 months before admission, confining him to bed. Electrocardiogram: no evidence of infarction; conspicuous ST depression. Mean control lysis-time 20·3 hours. Given chlorpropamide 250 mg. o.d. for 23 days. On the day after the start of the drug, the lysis-time dropped to 6 hours, and over the next 14 days it fell stepwise to 4 hours. On the 5th day of treatment, his pain ceased. After 10 days he was up and about, and he has remained symptom-free on moderate activity for $2^1/_2$ months. 6 weeks after discharge he was readmitted for 4 days for lysis-time measurements which varied between 5 and 6 hours. His lysis-time has, therefore, remained rapid, in spite of discontinuing the chlorpropamide.

Case 4.—Man, aged 51. Intermittent claudication of left leg for 2 years. Pain after walking 10–50 yards. Left foot colder than right. Both dorsalis pedis pulsations absent. Left posterior tibial pulsation barely palpable. Mean control lysis-time, 18·5 hours. After tolbutamide 500 mg. b.d., t.d.s., and q.d.s. the lysis-time fell only temporarily. After chlorpropamide 250 mg. b.d. it fell to 5–$7^1/_2$ hours with steady improvement of symptoms. When he was readmitted 9 weeks after starting chlorpropamide his lysis-times were 5–8 hours. Now after 4 months on chlorpropamide, he can walk several miles without pain. He continues to take 250 mg. o.d.

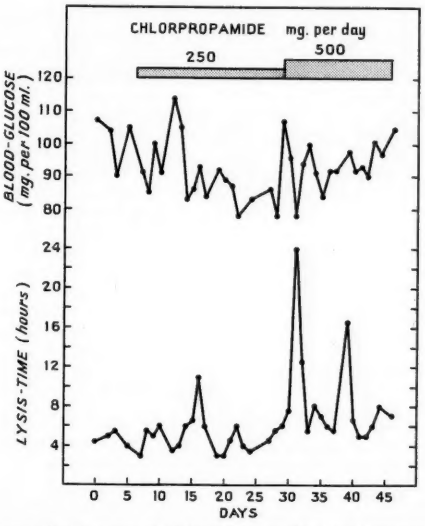

Fig. 3 (case 6)—Decrease of fibrinolytic activity by chlorpropamide when dosage was raised to 500 mg. daily in a man with intermittent claudication.

Case 5.—Man, aged 68. Intermittent claudication for 3 years. Began in left leg, for which 2 years before admission a left lumbar sympathectomy had been done with moderate benefit. Shortly after the operation he developed claudication in the right leg. At the time of admission he was able to walk 50 yards before halting from pain in right leg. Dorsalis pedis and posterior tibial pulsations absent in both legs. Mean control lysis-time, $5^1/_2$ hours. Given chlorpropamide 250 mg. daily. After 14 days the lysis-time was 2–3 hours. He was discharged on the above dose, but at follow-up $2^1/_2$ months later he was no better, in that although his right leg had improved he was now halted at the same distance as before by pain in the left leg.

Case 6 (fig. 3).—Man, aged 66. Intermittent claudication of both legs for 18 months. Pain after walking 200–300 yards. Both posterior tibial pulsations absent. Mean control lysis-time, 4·8 hours. Chlorpropamide 250 mg. daily was followed by a transient increase of lysis-time, and after 24 days the dose was increased to 500 mg. daily. After this, the lysis-time immediately increased, and the mean level over the next 18 days was 9·0 hours. This patient showed no symptomatic improvement, and chlorpropamide in a dosage of 500 mg. daily appeared to result in a definite increase of lysis-time and hence a reduction of blood fibrinolytic activity during the period of observation.

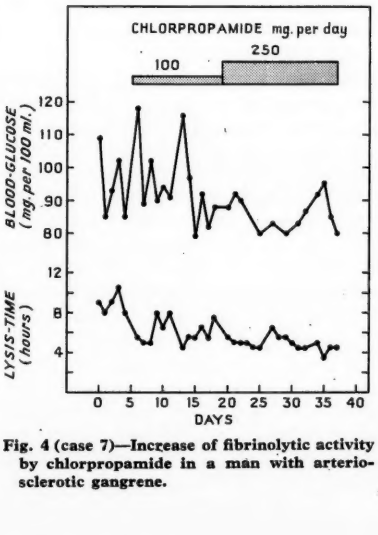

Fig. 4 (case 7)—Increase of fibrinolytic activity by chlorpropamide in a man with arteriosclerotic gangrene.

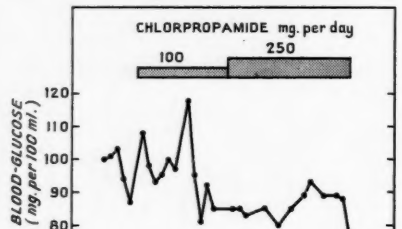

Fig. 5 (case 8)—Biphasic effect on fibrinolytic activity by chlorpropamide in a man with intermittent claudication.

When dosage was increased from 100 mg. to 250 mg. daily, the lysis-times were prolonged for 10 days, and then were reduced below the control levels.

Case 7 (fig. 4).—Man, aged 52. Early gangrene of toes of right foot with rest pain. 2 years before admission an above-knee amputation had been done for gangrene following embolism of the left popliteal artery. Since then increasing claudication of right leg, halting him at 20 yards. Popliteal and foot pulses absent on right ischæmic cyanosis of toes extending on to dorsum of foot. Mean control lysis-time, 9 hours. Chlorpropamide 100 mg. daily for 14 days was followed by a mean lysis-time of 6 hours. The dose was then increased to 250 mg. daily and during the next 18 days the mean lysis-time was 4·9 hours. During treatment his rest pain has diminished in frequency and there has been a definite reduction in the extent of ischæmic cyanosis, which is now confined to the distal halves of the toes.

Case 8 (fig. 5).—Man, aged 53. Intermittent claudication of left leg for a year, steadily worsening. Before admission pain halted him at 100 yards. Dorsalis pedis and posterior tibial pulsations absent on left. Mean control lysis-time, 7 hours. Given chlorpropamide 100 mg. daily for 14 days, during which period the mean lysis-time was 5·5 hours. The dose was then increased to 250 mg. daily, and this was followed by an increase of lysis-time for 8 days (mean lysis-time 8 hours). The lysis-time then fell for the ensuing 11 days (mean lysis-time, 3·7 hours). During the latter period, the patient's walking distance has increased from 100 to 400 yards and the pain has been less severe.

Comment

Of three patients given tolbutamide, one (case 1) showed a prompt increase of fibrinolytic activity and temporary symptomatic improvement, but became resistant to this drug; one (case 2) showed increased fibrinolytic activity and sustained improvement; and one (case 4) showed an inconstant fibrinolytic response, and was transferred to chlorpropamide, which was followed by increased fibrinolytic activity and symptomatic improvement.

Of six patients given chlorpropamide, two (cases 3 and 4) showed increased fibrinolytic activity and sustained improvement, both of which continued in case 3, in spite of cessation of the drug; two (cases 7 and 8) showed increased fibrinolytic activity, and to date improvement which can be classed as moderate; one (case 5) showed increased fibrinolytic activity but no improvement; and in one case (case 6) the drug appeared to reduce fibrinolytic activity.

Discussion

An oral means of enhancing spontaneous fibrinolysis has not hitherto been described. Though both tolbutamide and chlorpropamide appear capable of increasing the fibrinolytic activity of the blood, their mode of action is unknown. As there is no obvious correlation between the blood-clot lysis-times and blood-glucose levels, the observed increase of fibrinolytic activity does not seem to be a function of drug-induced hypoglycæmia. It is unlikely that nocturnal hypoglycæmia, causing release of adrenaline, was responsible for the increased fibrinolysis; for had this been so one would expect at least some of the fasting blood-glucose levels to be low. Furthermore, no patient experienced hypoglycæmic symptoms; these were specially inquired for and the blood-glucose levels were carefully watched because of the possible risk of severe hypoglycæmia to arteriosclerotic patients.

The magnitude of change in the lysis-times seems to be related to the pre-treatment levels, since those patients with long lysis-times showed the greater change. Too much should not be inferred from this, however, in the absence of knowledge about the relationship between lysis-time and fibrinolytic activity, which may not be linear. The reduction of lysis-time, which appears to be influenced by dosage (cases 7 and 8), may take 2 weeks to be fully manifest, as exemplified by case 3, where the lysis-time showed an initial steep reduction followed by a stepwise decrease over the next 14 days.

In two of the patients, chlorpropamide apparently increased the lysis-time. This increase was followed by a decrease below the control levels in patient 8, but not in patient 6—possibly because the measurements were not continued long enough. The biphasic response of patient 8 is reminiscent of a similar response to an injection of insulin in diabetics, and suggests the invocation of an opposing mechanism which may subsequently be overcome.

Because of the resistance case 1 acquired to tolbutamide, the biphasic response of case 8, and the negative response of case 6 to chlorpropamide, these results should be viewed with caution. They do not constitute sufficient evidence for the indiscriminate therapeutic trial of these drugs in arteriosclerotic conditions. But they do indicate that the fibrinolytic activity of the blood can be influenced by oral medication, and they are the first positive result from a number of pilot trials with various drugs undertaken by one of us in the past five years. The behaviour of chlorpropamide and tolbutamide merits further study (1) to determine whether either or both will enhance fibrinolytic activity for a long enough time to allow planned therapeutic assessment, and (2) to discover the frequency and duration of the negative effect encountered with chlorpropamide, a potential disadvantage. We would emphasise that diurnal variability, the known effects of exercise, and the possible effects of meals have made it necessary to confine this study, and probably future studies of these drugs, to inpatients, whose blood can be obtained fasting and under standard conditions of rest.

The investigation was designed to determine whether the sulphonylureas would increase the fibrinolytic activity of the blood, rather than to evaluate any therapeutic benefit which might ensue if this happened. The data are too few to permit clinical conclusions. Nevertheless, the improvement shown by some of the patients is not discouraging when taken in conjunction with the empirical observations of Singh and Bardhan (1959), who have reported improvement in 24 patients with angina pectoris on tolbutamide 500 mg. given nightly.

Summary

The oral exhibition of tolbutamide or chlorpropamide was followed by increase in the fibrinolytic activity of the blood (taken when fasting) in seven of eight arteriosclerotic patients. Of three given tolbutamide, one became resistant and another failed to respond, though he afterwards responded to chlorpropamide. Of six patients given chlorpropamide, four showed increased fibrinolysis; one showed a biphasic effect consisting of a reduction of fibrinolytic activity followed by an increase above the control levels; and in the sixth patient chlorpropamide seemed to decrease fibrinolytic activity during the period of observation.

The increases of fibrinolytic activity could not be related to the alterations of blood-glucose. The magnitude of change appears to be related to the control level of fibrinolysis, since those patients with initially long lysis-times showed the greater change.

Six of the eight patients showed clinical improvement, which was considerable in three and moderate in three.

A means of enhancing spontaneous fibrinolysis by oral medication has not previously been described. Further study is required to determine whether the sulphonylureas will be of value in arteriosclerotic diseases.

We wish to thank Mr. P. M. Birks for referring some of the patients with claudication and Miss Esther Gronow and Mr. John Evans for efficient technical assistance.

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TOLBUTAMIDE IN THE TREATMENT OF THROMBOANGIITIS OBLITERANS

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THE relief of anginal pain with tolbutamide in March, 1957 (Singh and Bardhan 1959), led to its trial in a case of thromboangiitis obliterans. The patient suffered from burning and gnawing pain in both feet, and had œdema of the right foot with ulceration and gangrene of the big toe, together with glycosuria of toxic origin. The result was a surprise. Within a week, though the glycosuria was unaffected, the relief from pain was very striking and the spread of gangrene appeared to be halted. Since then we have treated 36 cases of thromboangiitis obliterans with tolbutamide and, except in 2 cases of neuritic pain, the results have been consistently good.

Material and Method

The patients were all Indian men, 25 to 42 years old; and the duration of their disease was two to seventeen years. 24 were light to moderate smokers, but the others did not smoke. In 17 cases, after temporary relief from preganglionic sympathectomy, symptoms had returned in full. In 13 cases one or more limbs had already been amputated. According to their dominant clinical features, the cases could be grouped as follows:

Group A (4 cases).—Intermittent claudication.

Group B (5 cases).—Aching pains in the digits, instep, and ankle; intermittent claudication of moderate severity, lasting five to ten minutes; and coldness of extremities. Erythromelia in 3 cases; superficial phlebitis with discoloration of skin in 2.

Group C (3 cases).—Acute discomfort in the digits, instep, and ankle; more severe intermittent claudication lasting ten to thirty minutes; and coldness of extremities. Superficial phlebitis with discoloration of skin in 1 case.

Group D (7 cases).—Constant agonising burning or gnawing pain; coldness of extremities; and cyanosis of digits, in upper or lower, or both upper and lower limbs.

Group E (12 cases).—Constant agonising burning or gnawing pain; coldness of extremities; œdema; and ulceration and gangrene in one or more digits, in upper or lower, or both upper and lower limbs.

Group F (2 cases).—Paroxysmal lancinating pain in affected parts in patients with chronic disease.

Group G (2 cases).—Pain and swelling of stumps in amputated cases.

Group H (1 case).—Superficial phlebitis and pain and swelling of stump in an amputated case.

Tolbutamide 0·5 g. was given with breakfast, lunch, and dinner. All previous treatment (e.g., with nicotinic acid, ' Priscol ', or α-tocopherol) was stopped; and, as pain and discomfort diminished, analgesics were tailed off, and eventually discontinued.

When patients were free from symptoms, administration of tolbutamide was stopped so that the duration of relief without the drug could be assessed. On return of symptoms, a second round of treatment was given, followed by continuous maintenance therapy with 0·5 to 1·0 g. tolbutamide daily.

As there was no difficulty in assessing the relief of severe pain needing strong analgesics (e.g., pethidine and morphine) we did not use placebo controls in such cases. In patients with less severe symptoms, however, in whom the buoyant effect of the drug on the mind may have influenced the results, placebo tablets were given both before and for four weeks after initial tolbutamide therapy. Drug and placebo tablets appeared identical.

Results

The patients felt improvement two to five days after starting tolbutamide therapy and were symptom-free before the fourth week was over. Placebo controls were unaffected.

The agonising rest pain which had driven many a patient to amputation, and at least one of them to attempted suicide, was relieved. The relief was continuous and persisted throughout the day, surpassing in this way even the effect of repeated doses of morphine which had been given previously. Similarly, intermittent claudication was relieved; the limiting factors were now overexertion and crippling from amputation. Whether symptoms had recurred after sympathectomy, or whether gangrene was present, or whether response to analgesics, vasodilators, or α-tocopherol had been inadequate or nil, did not appreciably affect the benefit from tolbutamide. Even the stump pain disappeared. But the paroxysmal lancinating pain of neuritic origin, in 2 cases, did not respond.

Though there was no immediate change in arterial pulsation which could account for this relief, there was some flushing of the skin and the extremities felt warmer. Discoloration of skin, if present, disappeared and the accompanying superficial phlebitis subsided. Moist gangrene was more easily and quickly demarcated than is usual in this disease; the associated swelling of the hand or foot rapidly subsided; and when the dead tissues in digits peeled off, although the bare phalanges were sticking out, the wounds were remarkably clean and

tended to heal. In 2 cases with glycosuria this had not happened with adequate insulin therapy; and the effect of tolbutamide did not seem to be related to its hypoglycæmic action.

On discontinuing tolbutamide, relief of symptoms persisted for from one to seven weeks.

The general condition of the patients improved: they put on weight and were cheerful. There were no side-effects.

Illustrative Case

In June, 1957, a Hindu, aged 30, developed gangrene of both feet, following injuries. After left lumbar sympathectomy in December there was a temporary halt, but below-knee amputation of the left leg had to be performed in August, 1958. Right lumbar sympathectomy was done in September of that year, and above-knee amputation of the right leg a month later. Last December there was an acute flare-up in the right hand, with constant agonising pain, œdema, and gangrene of the thumb, index, and middle fingers, and glycosuria of toxic origin. Pulsation was very feeble in the right radial artery but present in the right brachial artery; pulsation in the left arm was normal. Though the glycosuria was fully controlled with insulin, this did not help the local condition. When insulin was stopped and tolbutamide ('Rastinon') therapy was started on January 5, 1960, the pain diminished from the fifth day; by the sixteenth day he was symptom-free, the gangrene was demarcated, and œdema of the hand had subsided. Later the dead tissues peeled off and the wounds were clean and dry; the phalanges, which were neatly sticking out, were removed. Relief is maintained with tolbutamide.

Discussion

We cannot yet explain the beneficial effect of tolbutamide in thromboangiitis obliterans. The intermittent claudication of ischæmic origin, the burning and gnawing pain due to thrombosis, and the pain, tenderness, and discoloration associated with thrombosis of veins are relieved, but the paroxysmal lancinating pain of ischæmic neuritis is unaffected. Similarly, in our experience, other pains of neuritic origin—e.g., pain of diabetic and alcoholic neuritis, tabetic pains, sciatica, and root-pains of spinal tumours—are not relieved; but patients with hemiplegia and parkinsonism benefit to some extent. A report by Gates and Hyman (1960) on the use of tolbutamide in paralysis agitans corroborates this.

The drug seems to have an anti-inflammatory action, judging by the subsidence of pain, swelling, and inflammation in areas where there was no obvious increase in blood-supply. In a case of rheumatic carditis, where low fever had persisted for several months in spite of salicylate and cortisone therapy, the temperature fell to normal within a week of starting tolbutamide, and the drug also controlled fever following severe measles. In both cases, the fever returned when tolbutamide was discontinued (after the temperature had been normal for three days) but subsided again when the drug was administered again.

On the analogy of the relief given by tolbutamide in angina pectoris (Singh and Bardhan 1959, Fabrykant and Ash 1960), it is likely that tolbutamide also prevents the local formation or accumulation of pain-producing metabolites.

As one of the characteristics of thromboangiitis obliterans is remission and exacerbation, the effect of tolbutamide maintenance therapy cannot yet be assessed; but 3 cases in which the disease was rapidly spreading and which have been treated for over two years have shown continuous clinical remission.

Summary

36 cases of thromboangiitis obliterans were treated with tolbutamide, 0·5 g. thrice daily with meals. Within three to four weeks there was spectacular relief of intermittent claudication and rest pain in the 34 patients who had these symptoms, but the neuritic pain of the 2 other patients did not respond. When tolbutamide therapy was discontinued, relief persisted for one to seven weeks. With maintenance therapy 3 cases have been in continuous clinical remission for over two years.

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THE XXX SYNDROME
FREQUENCY AMONG MENTAL DEFECTIVES AND FERTILITY

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As part of a wide investigation of chromatin-positive (XXY) Klinefelter's syndrome in Glasgow (Ferguson-Smith et al. 1957, Stewart et al. 1959) Ferguson-Smith (1958) surveyed most of the male population of Lennox Castle Mental Deficiency Hospital, and established that the frequency of XXY cases was rather over 1%. When the description by Jacobs et al. (1959, 1960) of their so-called superfemale with an XXX chromosome complement provided what seemed a feminine counterpart on the genetic side to the XXY Klinefelter's syndrome, it seemed logical to institute a similar search for cases of this type on the female side of the same mental deficiency hospital.

Investigation of the cases found has not yet been completed, but some points which have been already established deserve report.

Methods

Buccal mucosal smears were taken from as many as possible of the 637 female patients in the hospital, and 595 satisfactory preparations have so far been examined. These cases seem to be a representative sample of the varieties of mental defect seen in the majority of similar institutions in this country, although, owing to the policy of finding outside employment for as many patients as possible, we have seen relatively few of the highest grade of mental defectives.

FINDINGS IN 4 CASES OF XXX SYNDROME

Case no.	Age (yr.)	Intelligence quotient	% nuclei with sex chromatin		Chromosome no.	Maternal age (yr.)
			Single	Double		
1	30	50	43	30	47	28
2	39	58	50	25	47	35
3	61	38	35	33	47	40+
4	73	50	33	30	47	..

Buccal smears were stained by the original cresyl-echt-violet method of Moore and Barr (1955), a hundred suitable nuclei being examined in every case. Mitotic chromosome counts were performed in 3 cases on cultures of peripheral blood by the method of Hungerford et al. (1959) with some modifications mostly suggested by Miss Patricia Jacobs, and in 1 case on sternal marrow by the method of Ford et al. (1958).

Results

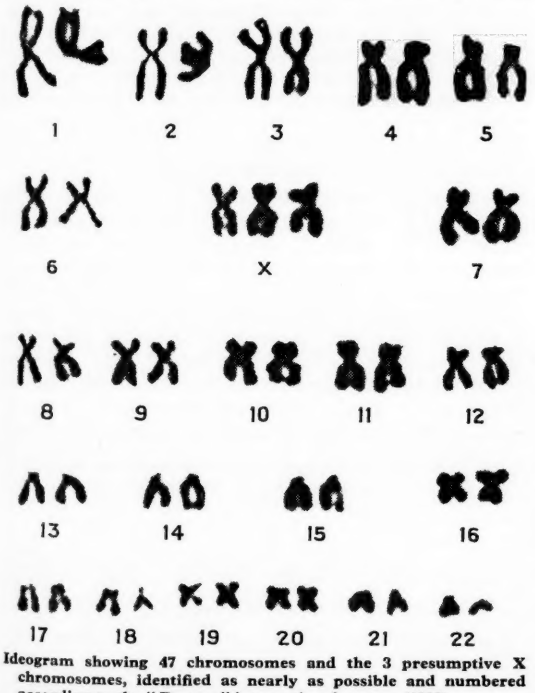
Of the 595 cases examined, 4 appear to be examples of the XXX syndrome (see accompanying table). Buccal smears from all 4 show the characteristic high count of chromatin-positive nuclei, many containing two sex-chromatin bodies.

In all 4 cases, chromosome counts showed a well-defined modal number of 47. In 3 cases preparations of sufficient quality to permit detailed analysis were obtained; and in these it was readily established that the extra chromosome is either an X, or at least something very near it (see figure).

These 4 cases present no very striking clinical features, and they stand out in no characteristic fashion from the general run of "non-specific" mental defect. All 4 patients are blood-group A, and all are epileptics; but these features may be coincidental. Family studies have so far disclosed nothing of note except high maternal age in 2 cases.

Fertility

Disregarding the oldest patient, whose previous menstrual history cannot be obtained, all appear to have a normal or nearly normal menstrual history. 1 of these patients, three years ago, gave birth to a single male child; and there is no doubt as to the maternity, as the child was born in the mother's present hospital. The child appears to be physically normal and of average intelligence. His mucosal smear is chromatin-negative, and blood-culture examinations show 46 normal chromosomes.



Ideogram showing 47 chromosomes and the 3 presumptive X chromosomes, identified as nearly as possible and numbered according to the "Denver" international system (1960).

Discussion

Our figures suggest that the frequency of the XXX syndrome among mental defectives is 0·7%. It is improbable that the frequency of XXX in the general population will approach this figure. The relatively high maternal age supports the view that non-disjunction is responsible for the chromosomal anomaly. The figure is rather lower than that for Klinefelter's syndrome. This may be a matter of chance; but it may be noted that, at least as far as non-disjunction at first meiosis is concerned, only maternal non-disjunction can give rise to an XXX zygote, so that one would expect the condition to be less common than XXY Klinefelter's syndrome.

It is disappointing to find so far so little evidence of a characteristic syndrome. In view of the normal menstrual histories, and the fertility of one of our cases, it is tempting to suggest that the extra X chromosome is producing no clinical effect at all, but it must at least be responsible for the mental deficiency.

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VENOUS THROMBOSIS DURING DEXTROSE INFUSION

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THROMBOSIS of veins during drip infusions depends on several factors. The most important are prolonged infusion (Bolton Carter 1951), and chemical irritation from rubber tubing (Handfield-Jones and Lewis 1952) or dextrose solutions (Brian and Grainger 1950). The problem has been reviewed by Jones (1957). The effects of rubber tubing can now easily be avoided by using disposable plastic giving sets. This makes it simpler to investigate the difficulties associated with the use of dextrose solutions.

Dextrose solutions are usually sterilised in the autoclave. This causes some hydrolysis, gluconic acid being

formed (Hudson and Tarlowski 1947). Völksen (1952) has suggested that acid should be added to the solutions to preserve their colour. Whatever the reasons, the solutions available commercially vary in pH from 3·5 to 4·5, and this acidity has been invoked as a cause of venous irritation and clotting. Attempts have been made to counter the acidity by buffering the solutions (Bolton Carter et al. 1952). Chemicals have been added to stabilise the dextrose during heating, or alternatively sterilising by filtration has been recommended (Brian and Grainger 1950).

The effect of acidity on thrombosis has been investigated. Bolton Carter et al. (1952) gained no benefit from buffering the solutions, but their test and control series were not concurrent. Page et al. (1952) found that buffering helped, but they used giving sets of various kinds, including rubber. McNair and Dudley (1959) devised an ingeniously controlled trial in which thrombosis was not reduced by using filtered solutions, but they admit that the number of cases was too small to be conclusive.

Aminoacid solutions are less irritant to veins when the pH is adjusted to 7·4 (Horvitz et al. 1943), and it seemed to us that dextrose might behave similarly. We therefore conducted a blind controlled trial of dextrose solutions sterilised by autoclaving or by filtration. We found that autoclaved solutions are acid and that they are associated with a significantly higher incidence of thrombophlebitis than are filtered solutions whose pH is near neutrality. We also attempted to answer several subsidiary questions, among them whether the use of giving sets for blood-transfusions before dextrose is infused increases the tendency to thrombosis. Our results confirm previous observations on the association of length of infusion with incidence of thrombosis. The final question of why acid-dextrose solutions cause venous thrombosis is still under investigation and will not be discussed further.

Methods

The patients studied were admitted under the care of two surgical teams at the London Hospital. Most patients underwent major gastrointestinal operations, but those with blood or biliary disorders were excluded. Each was randomly allocated to receive either autoclaved or filtered dextrose solution at operation, and neither observers nor patients knew which was given.

Plastic infusion sets only were used, and no other injections were given by this route. The technique of setting up the infusions was standardised as much as possible, using either a needle or short cannula, without cutting down. Signs of thrombophlebitis were recorded by the house-surgeon, using prearranged criteria. Cases were classified as " trouble free ", " thrombophlebitis ", or " minor difficulties ". " Minor difficulties " included all those which could not be definitely placed in the other groups. They were mostly instances of the drip stopping without apparent cause or because of subcutaneous leakage. Thrombophlebitis was diagnosed if a tender palpable cord or a red flare developed over the vein, in association with slowing or stoppage of the drip. This was a simple working rule, but it tends to underestimate the true incidence of thrombophlebitis.

The dextrose solutions were prepared in the same way, except that one was sterilised by filtration alone and the other was filtered and autoclaved. The bottles were specially purchased, coming from the same batch of glass. The rubber closures were all new, selected from the same batch, and subjected to the same preparatory techniques. Anhydrous dextrose from one batch was dissolved to make a 50% solution in distilled water. This was filtered through alkali-free (' Sterimat ' fibre) sterilising filter pads of SB grade into a sterile glass receiver. The bottles, containing 450 ml. of distilled water, were sterilised by heating in an autoclave. After cooling, 50 ml. of the sterile 50% dextrose solution was added to each bottle by an aseptic transferring device. The resulting solution was the filtration-sterilised 5% dextrose solution used in the trial. The autoclave-sterilised solution was prepared by adding 50 ml. of the filtered 50% dextrose solution to 450 ml. of distilled water in the giving bottle, and then autoclaving. In this way any material extracted from the bottle glass, the rubber closure, or the filter pad was common to both solutions. A similar technique was used to prepare 4% dextrose in 0·2 *N* saline.

Hæmolysis of stored citrated red cells by dextrose solutions was investigated in vitro. Measured volumes of stored blood were allowed to stand in tubes of dextrose solution at room temperature. These were centrifuged at intervals, and the hæmoglobin in the solution was measured in a colorimeter, using a green filter. A microscopic check was made to ensure that the solutions had been centrifuged long enough for red-cell envelopes to be removed.

TABLE I—THE RESULTS

Infusion	Thrombo-phlebitis	Minor difficulty	Trouble-free	Total
Autoclaved	20	4	7	31
Filtered	9	6	13	28
Total no. of infusions	29	10	20	59

Results

Fifty-nine patients were included in the trial. Table I gives the results according to the three categories already defined.

Because two teams were involved, and we suspected that the previous use of the giving set for blood-transfusion might affect the results, the data were classified further before statistical analysis to show the effects of these factors (table II). The comparison between autoclaved and filtered solutions shows that in each subgroup, thrombophlebitis was less frequent with filtered solutions. The difference between the incidence with autoclaved and filtered solutions, and the standard error, are shown in table II for each of the four subgroups. The weighted mean of these four differences (calculated by weighting each of the differences in inverse proportion to the square of its standard error) is 32% with a standard error of 12%, which is significant at the 1% level. This shows clearly that thrombophlebitis is more common with autoclaved than with filtered solutions.

By a similar analysis the difference between the two teams fails to be significant at the 5% level. Table II shows that for team A where the patient had had a previous transfusion of blood he was more likely to have thrombophlebitis after dextrose infusion, while for team B this was less likely. This contrast between the two teams is not significant, but it prompted a search for differences of technique. It was found that team A used the same giving set for glucose infusion after blood-transfusion, though it was rinsed quickly with normal saline. Team B changed their giving sets but not the needles after blood

TABLE II—INCIDENCE OF THROMBOPHLEBITIS ACCORDING TO TYPE OF DEXTROSE SOLUTION, TEAM, AND USE OF BLOOD

Infusion	Team A		Team B	
	Blood	No blood	Blood	No blood
Autoclaved	11/14*(*79%*)	5/7 (*71%*)	1/3 (*33%*)	3/7 (*43%*)
Filtered	5/11 (*45%*)	2/8 (*25%*)	0/2 (*0*)	2/7 (*29%*)
Difference (autoclaved—filtered) (%)	34	46	33	14
± standard error	±19	±26	±36	±26

* No of infusions with thrombophlebitis/total no. of infusions.

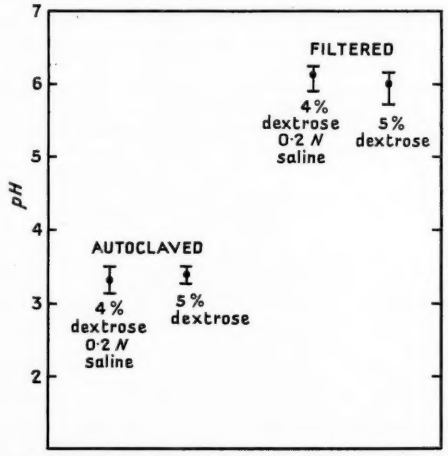

Fig. 1—Means and ranges of pH measurements from groups of five bottles selected randomly from autoclaved and filtered solutions used in the trial.

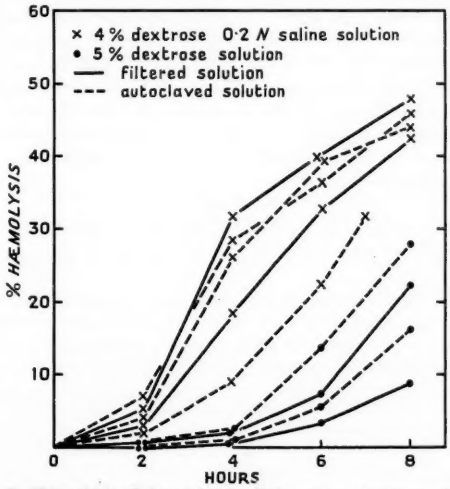

Fig. 2—Hæmolysis of citrated red cells in various dextrose solutions at room temperature.

had been given. This difference had not been noticed during the trial. When blood had been transfused the giving-set filter carried much red-cell debris and other solid material, and when this was placed in dextrose solution the blood on the filter lysed. The amount of blood was estimated, from the hæmoglobin released, to be about 5 ml.

Five bottles were selected at random from each type of dextrose solution used; the means and ranges of pH are shown in fig. 1 for dextrose and dextrose-saline. Investigation of the rate of hæmolysis of stored citrated blood in isotonic dextrose solutions showed that 4% dextrose in 0·2 *N* saline caused more rapid hæmolysis than 5% dextrose. The method of sterilisation (and hence pH) of the solutions had little effect (fig. 2). During the trial the dextrose-saline solution was used after blood-transfusion in nearly every case. Fresh red cells (heparinised) showed a similar but more delayed pattern of hæmolysis (fig. 3).

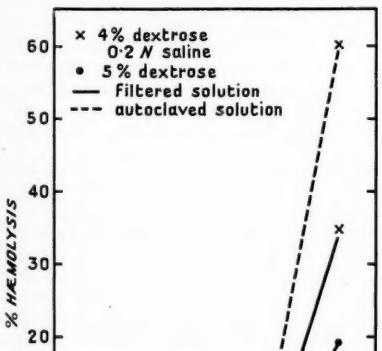

Fig. 3—Lysis of fresh red cells in various dextrose solutions at room temperature.

Team B had a lower incidence of thrombophlebitis both for autoclaved and filtered solutions (table II). This could be due to the shorter infusions (fig. 4), although this difference was not significant.

Discussion

Our results confirm the acidity of autoclaved dextrose solutions, and show that this was significantly associated with a high incidence of thrombophlebitis. Commercial dextrose solutions are often more acid than the ones used in this investigation. In one observer group the incidence of venous thrombosis reached 75%, but when filtered material was used it was only 36%.

Transfusion of blood before glucose infusion was associated with more thrombophlebitis, but only in one observer group. This was the group in which the same giving set was used for blood and dextrose solutions, and in which many patients must have received an infusion of broken-down red cells as already described. This effect did not reach significance—perhaps because of the small numbers in the trial. But the point seems worthy of further investigation since anything which favours red-cell breakdown is suspect as a cause of increased thrombosis.

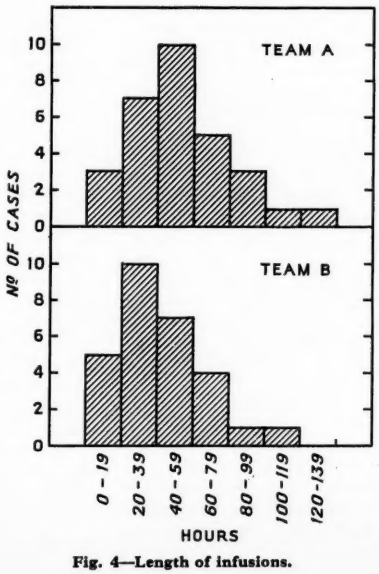

Fig. 4—Length of infusions.

In-vitro investigation of hæmolysis of stored red cells by dextrose solutions showed that it was more frequent with glucose-saline solutions than with glucose alone, and it is interesting that glucose-saline was the solution commonly used after blood-transfusion. The prevalence of hæmolysis following this procedure in children has been emphasised by Noble and Abbott (1959). Fresh red cells lyse in isotonic

dextrose solutions after 3–4 hours at room temperature, but we have also observed that fresh blood in paraffin-lined tubes readily shows hæmolysis within 5 minutes when rotated gently at 37°C with isotonic acid-dextrose solutions. This raises the possibility of hæmolysis in the vein used for infusion, but there is as yet no significant evidence of harmful effects from hæmolysis during dextrose infusion.

Summary

When thrombophlebitis follows infusions of dextrose solution the irritant factor is now likely to be the solution itself.

A controlled trial of acid and nearly neutral dextrose solutions (sterilised by autoclaving and filtration respectively) showed that thrombophlebitis is more than twice as common with the acid (autoclaved) solution.

The infusion of dextrose-saline after blood-transfusion through the same giving set causes hæmolysis in the blood retained in the filter, and these hæmolysed cells are injected with the infusion.

We are indebted to Mr. W. T. Irvine and Mr. J. E. Richardson, under whose care the patients were admitted, for help and encouragement; and to Prof. Clifford Wilson for much valuable criticism. Our thanks are particularly due to Mr. R. D. Cohen, Mr. J. J. F. Hamblin, and Mr. G. B. Winter, who recorded the clinical observations; without their meticulous help, together with that of many anæsthetists and nurses, the trial would not have been possible.

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New Inventions

A SUCTION TUBE FOR FREYER'S PROSTATECTOMY

SUCTION drainage for the Freyer's type of prostatectomy is often associated with leakage of urine and with introduction of infection. The appliances usually employed require frequent attention and adjustment.

The suction sump-drainage tube to be described has been used at Walton Hospital, Liverpool, and at other hospitals, on nearly 100 cases of Freyer's type prostatectomies over the past 3 years, and it has been found uniformly satisfactory.

The suction tube is made of polyvinyl chloride throughout (fig. 1). The outer tube, which corresponds in size to the Freyer's and Marion's tubes (30 HE size), is made in three lengths (marked on the tube)—i.e., 5, 5½, and 6 in. The inner (suction) tube is fixed by plastic "cement" inside the larger tube, with its lower end just above the level of the side hole; it emerges through the side of the outer tube at a point where a flap is made to support the bend of the inner tube. The inner tube, which is 6 ft. long, has an adaptor at the end for the suction apparatus. The top of the outer tube is closed by a cuffed rubber bung which can be removed for the extraction of adherent clot from its lumen. The air inlet is through the flap and a hole opposite.

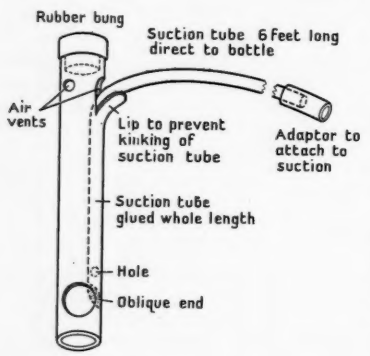

Fig. 1.

TECHNIQUE

The tube is sterilised by boiling, being coiled for this purpose and handled only by a ribbon.

The length of tube selected (usually 5–5½ in.) will to some extent depend on how obese the patient is. The correct size will allow the suction tubing to lie almost flush with the abdominal wall (fig. 2).

The prostate having been removed, and reasonable hæmostasis secured, the tube is inserted into the bladder in the usual way, and the bladder wall and wound are closed snugly around the tube, which is fixed to the skin by a nylon stitch.

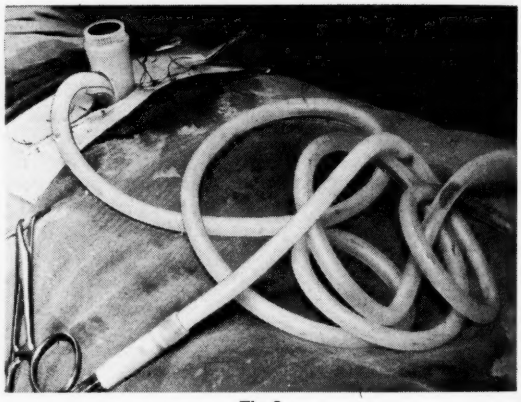

Fig. 2.

Suction is now started by means of the inner tube which is attached to a Poole or Simpson-Smith sucker; this will demonstrate that the suction is working and prevent wound soilage. If any small clots have formed they can be washed out by irrigating the suction tubing with saline or sodium-citrate (4·3% solution).

The dressing, preferably of a few layers of gauze, is now placed over the wound and fixed by strapping. The suction tube is strapped to the abdomen or upper thigh.

As soon as the patient reaches the ward the suction tubing is attached to a suction apparatus made by the Genito-Urinary Manufacturing Co., which should have been previously checked. This suction apparatus should keep the dressing dry, and the bladder free from introduced infection by avoiding repeated inspection and adjustment.

When the fluid sucked out is clear of blood, and the patient's general condition allows, the tube is removed and the wound is firmly dressed. A large Gibbon (size 9) or Foley (size 18F) catheter is passed into the bladder per urethram.

The apparatus can be used over and over again.

The tube is made by Portex Plastics, Ltd., Bassett House, Hythe, Kent.

My thanks are due to all the surgical staff at Walton Hospital for their help, and also to Mr. Jack Probert and Mr. William Keogh, theatre technicians, who made all the prototype tubes so skilfully.

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A STANDARD OBSTETRIC FORCEPS

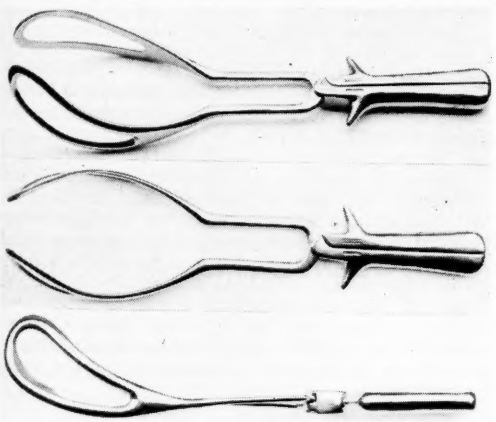
FORCEPS may vary in the important diameters which grip the fœtal head.[1] The variation is often seen between different patterns of forceps, but it may sometimes be seen in supposedly identical forceps. The reasons are that: (*a*) different manufacturers have different standard patterns; (*b*) modifiers of pre-existing forceps have often not laid down appropriate dimensions; (*c*) fœtal head sizes may have increased in the past 200 years; (*d*) most forceps are still handmade; and (*e*) modern writers of textbooks do not agree on desirable dimensions of forceps.

After measuring fœtal heads, and using Macdonald's figures [2] for fœtal-head size, theoretical dimensions for forceps for present-day practice were suggested. These, which were not regarded as final, were:

Distance apart of tips	3·0 cm.
Widest distance apart of blades	9·0 cm.
Length of blade	16·0 cm.
Radius of cephalic curve	11·25 cm.
Radius of pelvic curve	17·5 cm.
Length of shanks	6·25 cm.
Width apart of shanks	2·5 cm.

The length of the blade was measured in a straight line from the tip to the beginning of the shank.

There is no difference of note between the construction of these forceps and the general patterns in use, such as Simpson's, Ferguson's, Murray's, and Neville's (Kielland's forceps are standardised). But it was also decided to remove the extraneous clutter of the past two centuries and so simplify the forceps (see figure). In particular, the curve in the shanks



of the Barnes-Neville forceps, and indentations in heavy handles, are no longer necessary. Axis-traction devices have been discarded because the high forceps operation should not now be performed; this automatically does away with screws to hold the forceps together, and fishtail handles. A similar simplified forceps, devised by De Lee, is figured in Greenhill's textbook.[3]

Allen & Hanbury's Ltd. (7 and 8, Vere Street, London, W.1) have made a pair of forceps to the above dimensions. In use it was found that, because the widest diameter between the blades is slightly larger than that in most extant forceps, the tips of the blades bit into the baby's cheek and on one occasion caused a hæmatoma. The distance between the tip was therefore widened to 3·5 cm., and since that time they have caused no trouble in 18 months' continuous use at the Lambeth Hospital.

The object of this communication is to draw attention to the variation in measurements of present-day obstetric forceps, and to lay down what seem to be reasonable standards for those who would like them.

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2. Macdonald, I. *ibid.* 1953, **60**, 61.
3. Greenhill, J. P. Obstetrics. Philadelphia, 1955.

Reviews of Books

An Atlas of Anatomy and Surgical Approaches in Orthopædic Surgery

Vol. I: Upper Extremity. RUDOLFO CONSENTINO, M.D., assistant professor in orthopædic surgery, University of La Plata, Argentina. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960. Pp. 192. 84*s.*

IT is said that Abraham Colles, as a young boy, was playing in some deserted outhouses, when he came upon a discarded anatomical textbook. Its contents and vivid illustrations so fascinated him that thenceforth he could contemplate no other career than that of surgeon. What would he have made of Dr. Consentino's work? Here are none of the bold line drawings and multicoloured reticulations of most atlases. The author has depicted human anatomy by photographing a series of dissections—not, of course, a new idea, but the limitations of even an expert photographer and a patient dissector are such that it has very seldom been a practicable one. Many atlases include a few photographs, but this one contains almost 150 pictures of the upper limb, including 20 illustrating the structure of the hand.

Everyone who looks at this book and who has wielded a camera or a scalpel will want to congratulate Dr. Consentino on his results. The text might, in places, be more happily phrased, and the black-and-white format lacks the appeal to move another youthful Colles; but place before an orthopædic surgeon, refreshing his memory about some structures he is to expose on the morrow, this book and the conventional polychrome and often rather fanciful atlas, and there is no doubt which he will choose.

Atrial Septal Defect

An Investigation into the Natural History of a Congenital Heart Disease. H. GÖSTA DAVIDSEN, Rigshopitalet, Copenhagen. Copenhagen: Munksgaard. 1960. Pp. 225. D.Kr. 50.

IN this book Dr. Davidsen analyses postmortem reports of 190 cases of atrial septal defect which he has collected from the literature and describes 132 cases which he himself has studied clinically. His aim is to determine the natural morbidity and mortality of this condition as a yardstick for the assessment of surgical treatment. Though he presents a great deal of information about the postmortem and the clinical series, he is largely frustrated in his intention, as he admits, by the diversity of the defect and its complicating anomalies, and by the impossibility, now that surgery is established, of finding an adequate series of untreated patients. He has broken down his own series of 132 cases according to the anatomy of the defect, the presence of pulmonary hypertension, and the coexistence of other cardiovascular anomalies. Even in this large initial series, many of these special groups are too small to yield significant results.

The value of the analysis of the 190 necropsy cases is also doubtful. Dr. Davidsen admits that they are probably not typical of the condition as a whole, as is apparent from the high prevalence of associated anomalies—particularly lesions of the mitral and tricuspid valves. Probably many were reported because they were unusual, and are not typical of the general run of cases.

Though he has not achieved his main object, his extensive and thorough survey, and his selective and critical review of significant cases, will interest cardiologists. The figures are excellent, and the book can be recommended as a reference work.

The Divided Self

An existential study in sanity and madness. R. D. LAING, M.B., D.P.M., assistant physician, Tavistock Clinic, London. London: Tavistock Publications. 1960. Pp. 240. 25*s.*

THE first of a series of studies in existential psychology and psychiatry, this book is concerned with schizoid and schizophrenic persons, and its aim is to make madness and the process of going mad comprehensible. Looking at the schizophrenic

from the standpoint of existential phenomenology is an attempt to reconstruct the patient's way of being himself in his world, and gives a very different picture from that obtained by the psychiatrist who is looking at the schizophrenic as someone "diseased" who shows various clinical symptoms. As Dr. Laing remarks, "The behaviour of the patient is to some extent a function of the behaviour of the psychiatrist in the same behavioural field. The standard psychiatric patient is a function of the standard psychiatrist and of the standard mental hospital. The figured base, as it were, which underscores all Bleuler's great description of schizophrenics is his remark that when all is said and done they were stranger to him than the birds in his garden."

Dr. Laing postulates a need for the person to develop in early life a sense of ontological security, an abiding certainty of oneself as a person-for-oneself. Lacking this, the individual feels unsure of his real existence and of the validity of his inner real self. A "false self" is then developed, so that life can be carried on in apparent conformity with the outside world. The complications that ensue from the split between the inner-self and the false-self system, both in the schizoid person and the frankly psychotic, are discussed and feelingly illustrated by the author's clinical observations of his patients. They become beings less strange than Bleuler's birds as Dr. Laing shows us round the garden. Perhaps in another book we may learn about his relationship with these patients and his method of therapy: that should make equally fascinating reading.

Crash Injuries

JACOB KULOWSKI, M.D., F.A.C.S., F.I.C.S., attending orthopædic surgeon, St. Joseph's Hospital, St. Joseph, Missouri. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960. Pp. 1080. 260*s*.

IN 1899 a passenger, alighting from a New York street-car, was struck by an automobile and received injuries from which he died the following day. This was the first recorded motor-vehicle fatality in the United States; but a million and a quarter other deaths in that country have followed, and the total continues to rise at the rate of about a hundred a day. These deaths result from violent forces applied over a very short period. This book is a study of those forces, of the lesions they produce, and of the steps which can be taken to reduce them.

About a third of the volume deals with the mechanics of road accidents and such matters as the stress tolerances of the human body; the remainder is concerned with their clinical aspect and the treatment of various types of injury.

A great deal of interesting information is to be found in both sections. There can be no argument about the value of safety belts, but there is still some doubt as to the best pattern. Dr. Kulowski, perhaps because he is greatly concerned about hip and pelvic injuries, favours the lap-strap design. The driver who eschews a belt because he "never goes fast" should note that if his car hits a lamp standard at 30 m.p.h., he will be decelerated with a force which may exceed 170 *g*. On the clinical side, mouth-to-mouth resuscitation is now advocated in preference to all other methods by the American National Red Cross. But no device has yet been found to supplant the Thomas splint for the first-aid treatment of fractures of the shaft and upper end of the femur.

Portrait of Social Work

A Study of Social Services in a Northern Town. BARBARA N. RODGERS; JULIA DIXON. London: Oxford University Press (for the Nuffield Provincial Hospitals Trust). 1960. Pp. 266. 25*s*.

THIS is a report, with commentary and recommendations, of a survey of the social work carried on in a northern industrial town of 100,000 inhabitants "with a great deal of local pride". The authors set out numerical facts clearly, but shun jargon and statistical tables, and they have written a lively, readable, cursive book with the emphasis on those who do the work—their deployment, training (or lack of it), character, outlook, and relation to their chiefs, work, clients, other social workers, and social work in general.

Among those interviewed as likely to need help from social workers or to know of their work, general practitioners had only a sketchy knowledge of the scope of social work and almost no direct contact with social workers even in the health services. The authors' first plea is for making the principles and aims of social work more explicit. They believe that many more social workers should have a recognised training, both to improve their efficiency and, still more, to give them a professional outlook on themselves, their work, and their colleagues and professional status in the eyes of those who employ them or come in contact with them. Only the Government, the authors consider, can initiate the necessary reforms.

Ovum Humanum

LANDRUM B. SHETTLES, M.D., PH.D., assistant professor of clinical obstetrics and gynæcology, College of Physicians and Surgeons, Columbia University. New York and London: Hafner Publishing Company. 1960. Pp. 79. 55*s*.

IN this book Dr. Shettles seeks to fill the gap in the study of human embryology due to the paucity of direct observations on the human ovum during its growth, maturation, fertilisation, and the week of its preimplantation life. He has achieved his end by presenting a beautiful pictorial record of the human ovum's development during these early stages. The legends to the figures are in German, French, and English.

Essays and Studies, 1960

Collected by M. ST. CLARE BYRNE. Volume XIII of the new series collected for the English Association. London: John Murray. 1960. Pp. 114. 13*s*. 6*d*.

THOSE who regard litigation between doctors and patients, or their relatives, as a relatively modern phenomenon will be interested in Prof. C. J. Sisson's description of a legal action in which William Harvey was involved. In 1620 Harvey was one of a number of physicians asked to examine a wealthy man, Sir William Smith, afflicted with symptoms attributed to a stone. The other consultants urged that lithotomy be performed, but Harvey counselled conservative treatment, and the use of his own secret remedy. Within a few months (and after rejecting Harvey's advice, and undergoing an operation) the patient died. His executors refused to meet the doctor's bill, and the matter went to Chancery where Harvey eventually won his suit. A detailed account of the case is to be found in the first article in this book, the latest in a series of literary studies published for the English Association.

The Population Explosion and Christian Responsibility

RICHARD M. FAGLEY. New York and London: Oxford University Press. 1960. Pp. 260. 28*s*.

THIS book, by a minister of Congregational Churches, U.S.A., with special experience of international problems, purposes to bring home to readers, especially Christians of the Western Protestant churches, the menace of the sudden, violent, and progressive increase of world population, to which the word "explosion" quite accurately applies. Christians, Dr. Fagley urges, should, as a matter of great urgency, face the facts, frame an agreed policy, particularly on birth control, and press reluctant Governments and international bodies to take what action they can to stem the increase by means other than abortion, infanticide, famine, or war. Erudition, scholarship, and moderation pervade the book; every statement is authenticated and each quotation has its reference.

Medical readers may not feel like tackling the more theological chapters, good though they are; but medicine is no less responsible for the population explosion than is physical science for the atom bomb, and technical aids to controlling it must flow largely from medicine. The problem is therefore very definitely of concern to the profession, and any who doubt its reality or gravity or believe in easy remedies should at least read Dr. Fagley's first six chapters.

THE LANCET

LONDON 17 SEPTEMBER 1960

Future Maternity Hospitals

THERE is every indication that in the second decade of the National Health Service capital expenditure will be substantially increased. New hospitals will be built and old ones replaced. But the allocation of priorities will not be easy, for there has been no serious study of the country's overall need for hospital beds.[1–3] The situation in regard to maternity is probably clearer than most; for, however the number of beds needed for patients of certain ages or with certain diseases may wax or wane, women will certainly continue to have babies, and the demand for hospital confinement has risen steadily in the past twenty-five years.

Many of today's maternity hospitals have been converted from older buildings, or have developed piecemeal as the obstetric service, particularly the antenatal section, has evolved. This has led to some rigidity in design, with clear separation of antenatal and postnatal wards and usually a central delivery suite. Continuity of nursing and medical care is difficult, if not impossible, under these circumstances. STABLER [4] has suggested that the future maternity hospital should be built around a series of self-contained units of 10–15 beds, each with its own delivery room, but that a central operating-theatre should be retained. Throughout her pregnancy the patient would remain under the care of a small group of nurses and doctors attached to one of the units; and patients suspected of being infectious would be nursed on these units rather than in a separate isolation ward. This plan, though attractive in many ways, requires further study. The idea of nursing possibly infectious cases on the small units is unlikely to find much support. Mothers with undiagnosed infections are a source of anxiety and danger: tuberculosis and dysentery are two examples of maternal infections which may hazard the lives of newborn infants. A small isolation ward is still needed in any maternity hospital.

The issue of central or dispersed labour wards is crucial. Here there are two important considerations. First, close supervision by experienced midwives is essential in the labour ward. Owing to shorter working hours and arrangements for off-time and night duty, it is already difficult to maintain the necessary standard even in a central delivery suite. Dispersal is bound to raise fresh nursing problems. Secondly, unexpected complications may arise in labour and necessitate the patient's immediate transfer to the operating-theatre. Movement of a patient, particularly under an anæsthetic, from one part of the hospital to another is dangerous: corridors may be crowded at visiting-time, and the best of lifts may break down. On balance a central delivery suite next to the theatre is likely to be safer and more efficient. Possibly the architect, aware of these circumstances, can design small ward units in such a way that their delivery rooms are immediately adjacent to the operating-theatre. In this event the delivery rooms could be staffed by nurses either from the ward units or from the central operating-theatre. Experience would show which of the two arrangements is preferable.

At present babies are customarily nursed in cots by their mothers' beds; but each ward must have a small separate nursery with 2 or 3 cots for noisy babies at night and for other babies who require temporary cot-nursing apart from their mothers. The Central Health Services Council [5] has suggested that in each region special units for the care of premature and other abnormal babies should be restricted to a few of the larger maternity departments which cater for abnormal obstetrics. This is a realistic approach; for the necessary standard of nursing and pædiatric supervision cannot be maintained in small special nurseries scattered throughout the region. The Council suggest, too, that each special baby-care unit should have at least 20 cots—enough for a population of 200,000. These larger hospitals with special baby-care nurseries would accept women in premature labour and premature and other abnormal babies from other maternity hospitals and from domiciliary practice.

The small isolated maternity hospital is at an increasing disadvantage. Unexpected developments in pregnancy or labour may call for immediate attention not only by obstetrician and pædiatrician but also by physician, hæmatologist, blood-transfusion officer, biochemist, radiologist, anæsthetist, and others. Modern obstetric practice demands that maternity hospitals be sited immediately adjacent to general hospitals where these special skills are at hand. In his second Ingleby lecture, which we publish this week, Sir DUGALD BAIRD speaks of the great advantage, to a regional maternity service, of having a teaching hospital as its central point and a really close association with the public-health department. These are among many things he describes whose value, in everyday life, has been proved in Aberdeen.

Future hospital plans should take into account the need for general-practitioner beds, and this will involve administrative as well as planning difficulties. Many general practitioners oppose the recommendation of the Cranbrook Committee [6] that their beds should be under the general supervision of the consultant staff, and would opt for a separate autonomous unit close to the hospital. Such an arrangement would perpetuate the fragmentation of the maternity service. Much preferable would be a general-practitioner unit within the framework of the hospital, in which family doctors would accept the

1. *Times*, June 16 and 17, 1960.
2. The Demand for Medical Care. Nuffield Provincial Hospital Trust. London, 1960.
3. Creative Leadership in a State Service. The Acton Society Trust. London, 1959.
4. Stabler, F. E. *Lancet*, 1959, i, 299.
5. Report of the Central Health Services Council for the year ended Dec. 31, 1959. H.M. Stationery Office, 1960. See *Lancet*, July 9, 1960, p. 92.
6. Report of the Maternity Services Committee. H.M. Stationery Office, 1959. See *Lancet*, 1959, i, 397.

clinical discipline of the hospital as do all members of staff, including the consultants.

In its report the Cranbrook Committee set out the arguments for and against a unified maternity service based on the hospitals. Although the committee decided that this was not the time to alter the tripartite structure of the service, it clearly foresaw that spontaneous cooperation could lead eventually to integration and a unified service in which hospital and domiciliary practice would be complementary. Certain hospitals already have a satisfactory arrangement with their local medical officer of health whereby domiciliary midwives, during the antenatal period, visit selected patients who are booked for hospital delivery and take over nursing supervision when the patients are discharged forty-eight hours after delivery.[7] An interchange of hospital and domiciliary midwives, also contemplated by the Cranbrook Committee, would be a natural development of the early-discharge scheme. On the one hand this would give the hospital a more intimate link with the community it serves, and on the other it would provide the domiciliary midwife with greater opportunities for keeping abreast of advances in obstetric practice. This may be the future pattern of maternity care in the country, and it could be achieved with little or no increase in the number of hospital beds.

So far as maternity is concerned, any available capital might best be spent on replacing and re-siting the older hospitals. Today's patients are increasingly aware of the old-fashioned appearance of wards in which bathrooms are too few and privacy is lacking, of the failure to provide day-rooms where they can read or write in peace, and of the air of austerity which pervades the hospital.[8] Improvement in hospital design should be matched by a more sympathetic understanding of the mother's emotional needs.[9] A heavy responsibility rests on the shoulders of the senior medical and nursing staffs; for they, by their example and teaching, largely determine standard and the atmosphere throughout the hospital.

Anæsthesia for Neurosurgery

GREAT strides have been made in anæsthesia for neurosurgery; but the improvements have mostly resulted not so much from new physiological and pharmacological knowledge as from empirical application of established techniques. Our knowledge of the effects of drugs and techniques used in anæsthesia on that most vital factor—the bulk of the brain—remains hopelessly incomplete and confused. It was long believed that change in the cerebral blood-flow was the main determining factor: drugs which produced cerebral vasodilatation would increase the local blood-flow and thus the brain bulk; and so would agents which depressed respiration, since the accumulating carbon dioxide would exert a similar influence. Yet agents which are known to have these undesirable properties have been regularly recommended for neurosurgical anæsthesia. Thus WYLIE [1] some years ago reported excellent results with pethidine as a supplement to nitrous oxide and oxygen, even though pethidine undoubtedly depresses respiration and presumably promotes retention of carbon dioxide. The position as regards the lipoid-soluble supplements to nitrous oxide and oxygen is equally unsatisfactory. Trichloroethylene was long the standard agent for this purpose in neurosurgical work.[2 3] Yet it is well known to have vasodilator properties and to reduce the tidal volume in the presence of tachypnœa. The position with halothane is even more ludicrous; for this substance has far greater vasodilator activity than trichloroethylene and is beyond doubt a respiratory depressant, and yet despite these apparently undesirable properties many anæsthetists have found it to be a most satisfactory agent for neurosurgical anæsthesia.[4 5]

The wide acceptance of controlled respiration for certain types of neurosurgical anæsthesia is another indication of the present confusion, for the physiological basis for its use is obscure. Besides cerebral blood-flow the other main factor determining the pressure in the cranium is usually believed to be the pressure in the veins there; and this is said to be the pressure in the great vessels of the thorax minus the height of the head above the mediastinum. Controlled respiration must raise the pressure in the chest; for it substitutes for the normal recurring inspiratory increase in the intrathoracic negative pressure a rhythmic positive pressure which is transmitted in part to the mediastinum and no doubt to the vessels there. According to current theory, therefore, it will also raise the pressure in the cranial cavity. Some anæsthetists, indeed, believe that something of this sort happens and regard a respirator with a negative phase as essential.[6] HUNTER,[7] however, has indicated that the pressure swings produced by a respirator in the mediastinum are not accompanied by comparable changes in the intracranial pressure; and he has suggested that the veins in the neck, which are well known to fill and empty during normal respiration, act as a sort of reservoir in which changes in pressure are converted into changes in volume, with the result that the intracranial pressure remains largely uninfluenced by the modification in the breathing inherent in artificial ventilation of the lungs.

Apart from these basic considerations the success of controlled respiration in neurosurgery raises an important practical issue. For years surgeons and anæsthetists alike have used changes in the rate and character of respiration as a guide to the state of certain vital areas of the nervous system. In the paralysed and artificially ventilated patient, however, the surgeon can (at least in theory) invade those parts of the brain concerned in maintaining respiration without his receiving any warning of the trespass: this risk is perhaps greatest during

7. City and County of Newcastle upon Tyne: Annual Report of the Medical Officer of Health, 1959.
8. See *Times*, March 23, 1960.
9. See Morris, N. *Lancet*, 1960, i, 913.

1. Wylie, W. D. *G. ital. Anest.* 1951, **17**, 1.
2. Ballantine, R. I. W. *Anæsthesia*, 1956, **11**, 303.
3. McBurrows, M., Dundee, J. W., Francis, I. L., Lipton, S., Sedzimir, C. B. *ibid.* p. 4.
4. Brindle, G. F., Gilbert, R. G. B., Millar, R. A. *Canad. anæsth. Soc. J.* 1957, **4**, 265.
5. Campkin, V., Inglis, J. M. *Brit. J. Anæsth.* 1959, **30**, 586.
6. Galloon, S. *Anæsthesia*, 1959, **14**, 223.
7. Hunter, A. R. *Proc. R. Soc. Med.* 1960, **53**, 365.

removal of a large tumour in the posterior fossa. Surgeon and anæsthetist have to weigh the advantages and drawbacks of controlled respiration against those of the other methods of reducing the intracranial pressure, such as the sitting position, the administration of urea,[8] and ganglionic blockade.[9] It must not be assumed that a single technique will be satisfactory in all cases. An anæsthetic method which proves highly satisfactory for a patient with a pituitary tumour operated on in the supine position may be anything but satisfactory for a patient who has a posterior-fossa tumour removed in the sitting position. Perhaps we have tended to think too much in terms of anæsthesia for neurosurgery rather than of the anæsthetic technique appropriate for each of the many different operations undertaken by neurosurgeons.

Drug Treatment of Alcoholism

How useful are drugs in the treatment of alcoholism? In the withdrawal phase the main aims are correction of dehydration and malnutrition, and sedation. Vitamins (especially the B complex) are given in high dosage, at first parenterally and later orally (vitamin injections are also required in the treatment of certain complications, such as peripheral neuritis, Korsakow's psychosis, and Wernicke's encephalopathy). To calm the tense, anxious, agitated, and restless alcoholic, tranquillisers are now usually given, by injection or orally. Chlorpromazine,[10] promazine,[11] trifluoperazine,[12] other phenothiazines, and meprobamate [13] have all proved of value. The tranquillisers are at present the drugs most commonly used in the management of delirium tremens, although the old standby, paraldehyde, is still favoured by some. A few years ago, especially in the U.S.A., adrenal cortical extract and corticotrophin were often employed in the treatment of delirium tremens, but controlled experiments failed to show that "the results were superior to those obtained with . . . sedation, vitamins and other supportive measures".[14] Tranquillisers may also decrease the risk of withdrawal symptoms, though these are now rare [15 16] even after sudden complete withdrawal of alcohol. Phenytoin may also be given in order to prevent convulsions in this phase.

In the acute alcoholic stage sleeplessness is often troublesome, and hypnotics may be necessary. Many alcoholics are prone to use to excess any sedative or stimulating drug [17]—in particular the barbiturates and paraldehyde, but also meprobamate, amphetamines, and phenmetrazine. On the whole, therefore, non-barbiturate hypnotics, such as thalidomide, methpyrlone, and glutethimide, are preferable, though even these are not free from the risks of habit-formation and addiction.[18]

8. Stubbs, J., Pennybacker, J. *Lancet*, 1960, i, 1094.
9. Hewer, A. J. H. *Proc. R. Soc. Med.* 1952, **45**, 431.
10. Feldman, D. J. *Med. Clin. N. Amer.* 1957, **41**, 381.
11. Browne, I. W., Ryan, J. P. A., McGrath, S. D. *Lancet*, 1959, i, 959.
12. Cohen, S., Ditman, K. S., Mooney, H. B. *in* Trifluoperazine (edited by H. Brill). Philadelphia, 1958.
13. Sargant, W. *Brit. med. J.* 1958, ii, 1095.
14. Berman, L. H. *Quart. J. Stud. Alc.* 1956, **17**, 28.
15. *Wld Hlth Org. tech. Rep. Ser.* 1955, **94**, 7.
16. Glatt, M. M. *Brit. med. J.* 1955, ii, 738.
17. Glatt, M. M. *ibid.* 1958, ii, 1100.
18. Glatt, M. M. *ibid.* 1959, i, 50.

Administration of disulfiram is usually restricted to long-term treatment; but MARTENSEN-LARSEN,[19] who was the first to administer this drug to alcoholic patients, also recommended it (in combination with the anti-histamine promethazine and sodium chloride) as the treatment of choice for intoxication.

The tranquillisers are sometimes used also in the long-term management of alcoholism for purposes such as helping the "dry" alcoholic over periods of anxiety and tension and encouraging him to keep in regular touch with the therapist. Undue dependence of alcoholics on any drug, however, should be avoided. Only three of the many substances recommended in the past as aiding the alcoholic to maintain sobriety are now in more or less widespread use. Probably the most popular is disulfiram.[19] This inhibits the breakdown of alcohol at the acetaldehyde stage. Thus if, having taken disulfiram, the patient consumes alcohol within the next three days or so, he may experience extremely unpleasant or even life-threatening symptoms. The knowledge of the risks involved (or the experience of a disulfiram-alcohol test carried out in hospital) is in most cases enough to deter the patient from drinking so long as he continues to take the tablets. The minimal maintenance dose varies from case to case. Special caution is needed in the presence of such conditions as heart-disease or liver cirrhosis; and on no account must the drug be given without the patient's knowledge (there have been instances where the tablets have been added to the alcoholic's tea by his desperate wife). Many have found disulfiram an excellent adjunct even though for the alcoholic it is often easier to give up taking the tablets than the alcohol. But then no treatment can be expected to succeed unless some motivation to stay sober is present from the start or is induced by psychotherapy.

In recent years another substance, citrated calcium carbimide (C.C.C.) [20] has been used with the same aim as disulfiram. Sensitisation to alcohol occurs sooner with C.C.C. than with disulfiram, the alcohol reaction and the side-effects are milder, and the "protection" afforded does not last so long.[21 22]

Emetine is another drug often used in alcoholism. The aim here is to produce an aversion against the sight, smell, and taste of alcohol. On a series of occasions, separated by rest periods, the drug is injected and shortly afterwards alcohol is drunk, so that in time a conditioned reflex is established.[23 24] Finally, apomorphine is sometimes injected to induce aversion, as with emetine. But DENT,[25] the main advocate of apormorphine treatment in this country, strongly disagrees with this view and maintains that the drug works mainly by allaying anxiety and craving. DENT has also devised a simple method of giving apomorphine by mouth (without subsequent administration of alcohol) to outpatients and in general practice.

19. Martensen-Larsen, O. *Quart. J. Stud. Alc.* 1953, **14**, 406.
20. Ferguson, J. K. W. *Canad. med. Ass. J.* 1956, **74**, 793.
21. Armstrong, J. D. *ibid.* **77**, 228.
22. Glatt, M. M. *J. ment. Sci.* 1959, **105**, 476.
23. Voegtlin, W. L., Lemere, F. *Amer. J. ment. Sci.* 1940, **199**, 802.
24. Williams, L. Alcoholism. Edinburgh, 1956.
25. Dent, J. Y. Anxiety and its Treatment. London, 1955.

No one form of therapy will produce the best results in every alcoholic.[26 27] Individual assessment should be followed by a combination of psychological, physical, and social techniques; and the contribution which Alcoholics Anonymous can make should not be forgotten. The doctor's attitude to the patient may be more important than the drug he prescribes. The training of medical students in the treatment of alcoholism is often sadly deficient; but, even so, there is little excuse for pretending that this disorder can be treated by dispensing moral exhortations and barbiturate tablets.

Annotations

SHORTAGE OF DIETITIANS

A DIETITIAN is needed in a general hospital if patients are to benefit from present-day knowledge of nutrition. The role of dietitians may have become less prominent in the management of peptic ulcer; but careful dietary control is needed in some illnesses—particularly heart-failure and hepatic disease. The dietitian greatly facilitates the work of the diabetic clinic, and she has useful work to do in advising pregnant women and mothers of young children on correct feeding. Moreover, she can make a real contribution as a nutritionist by working with the catering officer and by lecturing to the nurses on proper feeding in health and disease.

King Edward's Hospital Fund for London has recently published a memorandum on the Shortage of Dietitians[28] based on discussions held with interested parties including doctors, dietitians, the Ministry of Health, and the Royal College of Nursing. Concurrently an investigation was undertaken jointly by the Fund and the Ministry of Health into the present work of dietitians in the hospital service, and this is reported in part II of the memorandum.

Unfortunately only a few hospitals today can provide a full dietetic service, and the increasing shortage of dietitians has now become very apparent. A survey of the fourteen hospital regions of England and Wales showed that there were only 95 therapeutic dietitians or caterer dietitians. There is, however, a greater concentration in provincial and London teaching hospitals, where 112 were employed. Fortunately, despite the shortage of dietitians the subject is not entirely neglected, as interested ward sisters and catering officers often make a substantial contribution to dietetics in a hospital, but beyond doubt a great many patients in British hospitals are not getting the full benefit of modern nutritional knowledge.

Several factors have contributed to the present shortage of dietitians. An important one is the length of training. There are two avenues. For the first a preliminary qualification, consisting of one of the following, is needed: a degree in pure science, household science, or nutrition, a domestic science teacher's diploma, an institutional management diploma, a specified catering diploma, or training or State registration in nursing: and this is followed by a dietetic diploma course of 15–18 months. Alternatively, there is a dietetic course of 4 years' duration. It is now widely felt that what is needed is a properly integrated course of training lasting 3 years or perhaps even less. Furthermore the salary scales have been unsatisfactory, and there has been a substantial drift from the hospital service into the school meals service or industry. A salary scale based only on the number of assistants is never satisfactory, and this arrangement may have helped to bring about the excessive concentration of dietitians in relatively few hospitals. Medical staffs must accept some responsibility for the present difficulties, for their interest or indifference makes a great difference to the success of the dietetic department.

The modern dietitian has much more to offer than the supply of a few weighed diets; and, if allowed to, she can make a very valuable contribution in the outpatient department and on hospital nutrition in general. A hospital which does not enable the dietitian to take her meals with the ward sisters cannot expect to retain the services of an intelligent, well-trained person. There is much to be said for the medical staff committee nominating one of its members to help a new dietitian in coordinating her work and in dealing with the initial administrative problems.

PORPHYRIA IN IRELAND

THE least common of the porphyria group of diseases is congenital porphyria; yet the first recorded case of porphyria, reported in 1874,[1] was undoubtedly of this type. Since then only 48 such cases have been described. Apart from sunlight, non-genetic factors are unimportant in precipitating the symptoms of congenital porphyria. On the other hand, in acute intermittent porphyria, though the disorder often develops spontaneously, precipitating factors, especially drugs, are important. In 1889—a year after the introduction of sulphonal—Stokvis [2] reported a case of acute porphyria in an elderly woman who had taken this drug; and other such reports followed. The introduction of barbiturates in 1903 led to a similar crop of cases of acute porphyria.

Studies of acute porphyria, and to a lesser extent of porphyria cutanea tarda,[3] have revealed an apparent increase in their prevalence. A striking fact is that in both Sweden and Australia the prevalence of acute porphyria is about 1·5 cases per 100,000; whereas in Northern Lapland and in South Africa the figure is much higher—1 per 1000 and 1 per 100 respectively—because in each of these regions an early prolific ancestor carried the genetic trait.[3]

Fennelly et al.[4] find that up to 1950 no case of porphyria had been described in Eire; but they now list 50 reported cases, including fourteen families with acute porphyria and one with porphyria cutanea tarda. This gives a prevalence in Eire of 1 in 80,000 of the total population, which is about the same as in Australia and Sweden. The prevalence in Northern Ireland may be higher—possibly 1 in 5000, according to Stevenson.[5] These figures include latent cases of acute porphyria and of porphyria cutanea tarda—that is, subjects with the genetic trait, who excrete porphobilinogen or porphyrins respectively, but who have no symptoms. The clinical picture of these diseases in Eire differs in no way from that of acute

26. Wallerstein, R. S., Chotlos, J. W., Friend, M. B., Hammersley, D. W., Perlswig, E. A., Winship, G. M. Hospital Treatment of Alcoholism. London, 1957.
27. Glatt, M. M. *Lancet*, 1955, i, 1318.
28. Memorandum on the Shortage of Dietitians. Pp. 38. 2*s*. Obtainable from King Edward's Hospital Fund for London, 34, King Street, London, E.C.2.

1. Schultz, J. H. Ein Fall von Pemphigus leprosus, kompliziert durch Lepra visceralis. Greifswald, 1874.
2. Stokvis, B. J. *Ned. Tijdschr. Geneesk.* 1889, **2**, 409.
3. *Lancet*, 1959, ii, 93.
4. Fennelly, J. J., Fitzgerald, O., Hingerty, D. J. *Irish J. med. Sci.* 1960, p. 130.
5. Stevenson, A. C. *Radiation Res.* 1959, **1**, suppl. 1, p. 306.

porphyria[5 6] and porphyria cutanea tarda[6 7] in England and Scotland. Fennelly et al. stress the dangers of barbiturates, especially barbiturate anæsthetics, but agree with Goldberg[5 6] that only in those with the genetic trait may an acute attack be precipitated by barbiturates.

Any notable increase in the prevalence of the genetic trait, as in South Africa, will require many generations; but the introduction of a widely used drug which adversely affects porphyrin metabolism might significantly change the incidence of the active disease. For this reason, those treating porphyria families should be particularly circumspect in administering any new drug.

MUSCLES OF RESPIRATION AND SPEECH

IT is generally assumed that the intercostal muscles as well as the diaphragm take part in normal quiet respiration and that expiration is passive. Clinical experience shows that respiration can be maintained without active diaphragmatic movements. From the way in which the intercostal muscles are attached to the ribs it was believed that the external intercostals raise the ribs and increase the diameter of the thoracic cavity, and so act as inspiratory muscles; and that the internal intercostals are used only in vigorous expiration or to maintain the distance between individual ribs. These same muscles, and others, must also be concerned in the precise regulation of expiration necessary in speaking and such occupations as playing wind instruments.

Obtaining direct information about each muscle calls for ingenuity and skill on the part of the investigator and a certain hardihood on the part of the subject. The best direct proof that an unseen muscle is contracting is the appearance of action potentials recorded from leads attached to electrodes inserted in the muscle. The difficulty about applying this technique to the intercostals is that they form two thin closely contiguous sheets of muscle whose movements are such that the sheets tend to slide in opposite directions, but there are areas where one or other muscular sheet is deficient and the remaining one can be observed without difficulty. The diaphragm forms a dome over the abdominal viscera; and when needle electrodes are inserted into it care must be taken to avoid the viscera and pleural cavity.

An ingenious way of circumventing this difficulty is for the subject to swallow the electrodes till they come to lie at the plane where the œsophagus passes between the diaphragmatic crura.[8 9] Accurate information about intratracheal pressures can be obtained by passing a small balloon and tube through the nose till the former lies behind the posterior soft part of the trachea just above the bifurcation. Check experiments have shown that these techniques give reliable information. When air is lost only slowly through the mouth, then mouth pressure reflects intratracheal pressure. For wind-instrument players a manometer can be used, connected to a small tube which passes through the corner of the mouth and does not disturb lip work.[9 10]

Finally all these measurements have to be correlated with the phase of respiration. Where speech is to be studied, obviously any form of spirometer or pneumotachograph is out of the question. Instead the subject can be inserted up to the neck in a large plethysmograph which records the air displaced from the tank during respiration.[8 9] By combinations of these techniques it has been found that in quiet breathing the diaphragm is almost wholly responsible for inspiration, and that action potentials appear in it before the inward flow of air begins.[11] Apparently the external intercostals are not used in quiet inspiration, but an upper part of the internal intercostals, where the muscles are not covered by the external layer, is used. A lower part of the internal intercostals contracts during expiration. In addition, diaphragmatic activity does not cease until some time after expiration has begun.[11] Thus quiet expiration is not, as was formerly thought, a wholly passive process. In forceful breathing both external and internal intercostals are used and the transversus thoracis aids in expiration,[11] as well as all the large accessory muscles such as latissimus dorsi, rectus abdominis, and external oblique.

For speech, air has to be expired in regulated bursts in order to make the various sounds, and each expiration must last long enough to give meaning to phrases. Singing and the playing of wind instruments demand even finer control of rate of air-flow and pressure of supply in order to regulate the volume and quality of sound produced. In quiet talking tracheal pressure is of the order of 2 cm. water, and a parade-ground shout raises this to between 20 and 30 cm. water.[9] If loudness is kept constant tracheal pressure must also be maintained, despite a steadily decreasing volume of air in the lungs. The necessary pressure is produced by the thoracic muscles which oppose the natural elastic recoil, or compliance, of the lungs and chest wall. At the beginning of speech with full lungs, the external intercostals hold the thorax in a slowly declining " open position "; then their activity decreases unit by unit, and overlaps with the onset of activity in the internal intercostals which slowly compress the lungs in order to maintain the required steady pressure. As the lungs empty still further, other muscles are brought in to help keep up the pressure—for example, latissimus dorsi and, at the end of a long phrase, rectus abdominis.[8 9] The louder the utterance the earlier the expiratory muscles must begin to contract. Apparently, in most people during speech the diaphragm shows little activity and expiratory control depends on coordination between the external and internal intercostals. The object throughout is to regulate pressure below the vocal cords. Paraplegics use any available muscle—commonly, for example, latissimus dorsi. With a high spinal injury adduction of the scapulæ can be used.[9]

The pitch of a voice depends on the tension in the vocal cords, and this is adjusted by means of the intrinsic laryngeal muscles before any audible sound emerges. The controlled intratracheal pressure forces air past the glottis, and separates the margins of the cords setting up a series of vibrations and recoils. These facts were ascertained by inserting fine needles in the laryngeal muscles and recording the action potentials.[12]

The internal intercostals seem to be used a great deal in making fine pressure adjustments in speech and enabling stresses to be made. They go into activity measurably before speech begins and can fluctuate almost as rapidly as the small muscles of the hand.[8 9] Other respiratory muscles do not show the same rapid variation in activity. In some subjects the external intercostals exert a check action after a stressed syllable and thus momentarily oppose the outward air flow induced by the

6. Goldberg, A. *Quart. J. Med.* 1959, **28**, 183.
7. Holti, G., Rimington, C., Tate, B. C., Thomas, G. *ibid.* 1958, **27**, 1.
8. Draper, M. H., Ladefoged, P., Whitteridge, D. *J. Speech Hearing Res.* 1959, **2**, 16.
9. Draper, M. H., Ladefoged, P., Whitteridge, D. *Brit. med. J.* 1960, i, 1837.
10. Faulkner, M., Sharpey-Schafer, E. P. *ibid.* 1959, i, 685.
11. Taylor, A. *J. Physiol.* 1960, **151**, 390.
12. Buchthal, F. *Quart. J. exp. Physiol.* 1959, **44**, 137.

internal intercostals. At a fairly regular interval after internal intercostal activity begins, tracheal pressure increases and then sound follows.

A skilled player of a wind instrument uses the same muscles as a singer or a speaker, but far more often he has to produce a large volume of sound—that is, a high intratracheal pressure. An expert trumpet player on a loud top note produces an intratracheal pressure of 80 mm. Hg, or even occasionally 160 mm. Hg; the oboe often demands 60 mm. Hg, the clarinet and French horn somewhat less, and the flute least of all.[9 12] In fact, the problem with the flute is to maintain long phrases at a low pressure, in contrast with the trumpet, which may need long phrases at high pressure. When playing the trumpet, as may be imagined, considerable circulatory changes are inevitable and dizziness or blackout can occur from the equivalent of the Valsalva manœuvre.[12] Yet these pressures are nothing compared with those produced by a violent cough in a muscular subject, when the intratracheal pressure may be as high as 200–450 mm. Hg.[12]

ADDER-BITES AS A HOLIDAY HAZARD

ADDER-BITES are becoming commoner in the south of England as a result of the influx of holidaymakers. The increase is attributable partly to the tent, caravan, or bed-and-breakfast, with its compulsory outdoor meals and lack of sanitation: the holiday season from July to mid-September coincides with the breeding season of *Vipera berus*. Adders are extremely local in their habitat; some country practitioners in Cornwall have never seen a case of adder-bite in thirty years' practice, while one not ten miles away treats at least 3 a year. In a review of the past eight years in Cornwall, Morton [1] has reported 18 cases. All the bites were on the extremities, and of 12 cases seen by him personally only 4 were accidental; the other 8 followed attempts to capture the snake under the impression that it was a harmless grass snake.

The only death associated with snake-bite in England in the last nineteen years was attributed to cardiovascular collapse from anaphylaxis due to the serum given a few minutes earlier.[2] The venom of *Vipera berus* is not very toxic: for a 600 g. guineapig the M.L.D. is 40 mg., compared with 1 mg. of Russell viper venom. The venom of *Vipera berus* contains a small amount of neurotoxin to paralyse its prey and facilitate swallowing it whole. Hæmorrhagins are also present. Hæmorrhagin has a special affinity for the endothelial cells of the capillaries, causing lysis of the cells and subsequent hæmorrhagic œdema or small petechiæ; sometimes a canary-yellow discoloration of the skin spreads up the course of the lymphatics, and in 1 of Morton's cases this involved the whole upper limb. In his series no sloughing of tissues was seen, so the cytotoxins which are partly responsible for the œdema are not very powerful.

The best and safest first-aid treatment is to delay the absorption of the toxins up the lymphatics—in the upper limb by a sling and bandage, and in the lower limb by tying the two legs together and keeping the patient in the recumbent posture. The results of an adder-bite are completely unpredictable since they depend on the amount of venin injected and on the age and constitution of the patient. The local effects are constant in kind but variable in intensity. General effects may be negligible in adults. The earlier the onset of such effects the more severe will these be and the greater the local reaction to the bite. In severe reactions giddiness, sweating, collapse, and severe persistent vomiting ensue within the hour; and Morton finds that, if these symptoms have not developed within two hours after the bite, no antivenin is necessary: rest, reassurance, and the administration of an antihistamine drug at intervals of from four to six hours is all that is required.

The old-fashioned tissue-damaging measures, such as the tourniquet, incisions, and suction, rubbing in potassium-permanganate crystals, and infiltration with 5% carbolic soap, have no place in the treatment of adder-bites in this country. The antivenin available in all public-health laboratories is the Pasteur Institute E.R. serum in ampoules of 10 ml. for neutralising the venoms of vipers in France (*Vipera berus* and *Vipera aspis*). This should be given subcutaneously in the vicinity of the bite, if the anatomical site allows, but never in the fingers or toes. Since most bites are on the fingers, and the cases are rarely seen early the serum must often be injected intramuscularly into the buttocks. Serum sickness develops commonly, despite administration of anti-histamine drugs. The antivenin controls the general symptoms in from two to twelve hours after its administration, and in only 1 case in Morton's series was it necessary to give glucose-saline intravenously on account of shock.

Morton calls for propaganda in the Press, through television, and in the schoolroom to bring this holiday hazard to the notice of the public.

1. Morton, T. C. *Brit. med. J.* July 30, 1960, p. 373.
2. See *Lancet*, 1957, i, 1095.

ARTHROPOD-BORNE VIRUSES

IN Britain our wont is to complain about the weather, but it is worth considering some of the advantages of our temperate, if uncertain, climate. One advantage is our almost complete freedom from virus diseases spread by the bites of blood-sucking insects. The Scots and the Irish may occasionally be bitten by ticks which carry the virus of louping-ill, and may then have a mild influenzal illness or a more serious disease resembling poliomyelitis; but in England we seem to be free from all such hazards. Our good fortune is the more remarkable because more than a hundred distinct animal viruses are spread by arthropods —mostly mosquitoes. Where do all these viruses come from? How important are they as possible causes of disease in man? These and other questions were discussed at a symposium held by the Royal Society of Tropical Medicine and Hygiene.[1]

Prof. C. D. Darlington suggested that as regards the virus the distinctions between animals, insects, and plants were not fundamental, but that the fundamental distinction was between the form of nucleic acid which was the basis of propagation. He contrasted the mechanism whereby the genetic apparatus of an organism was passed on to its descendants and the means by which infection was transmitted from one organism to a second. He suggested that vectored viruses of animals and bacteriophages were examples of double systems of propagation which depended on both heredity and infection.

Mr. P. F. Mattingly developed the thesis that the arthropod-borne viruses arose in their arthropod vectors. Within the insect they might have arisen de novo or by parasitic degeneration from higher forms—possibly rickettsiæ. In either case it seemed probable that the present form was developed in association with the

1. *Trans. R. Soc. trop. med. Hyg.* 1960, **54**, 89–134; see *Lancet*, 1960, i, 319.

evolution of blood-sucking habits by arthropods. Most of the vectors of these agents are species of culicine mosquitoes which are primarily bird-feeders. He therefore suggested that the earliest forms had arisen in culicine mosquitoes and in birds, and that spread to mammals was a later development. He emphasised the importance to the virus of hibernation or æstivation of mosquitoes in subtropical areas where climatic conditions limit mosquito activity.

Dr. C. E. Gordon Smith declared that many arthropod-borne viruses were not known to cause any disease in man but that man could become infected by intruding into certain ecological backgrounds, as in the case of human infections with " jungle " yellow fever.

Dr. C. H. Andrewes supported Mr. Mattingly's view that the arthropod-borne viruses probably arise in association with their insect vectors, but suggested that the tick-borne viruses were more primitive than the mosquito-borne. The transovarial transmission of viruses of the Russian spring-summer encephalitis group (which includes our virus of louping-ill) indicated a very old partnership between tick and virus.

Prof. D. S. Bertram suggested that the explanation of transovarial transmission with ticks but not with mosquitoes lay in the presence in the former of only one membrane separating the ovary from the hæmocele, whereas in mosquitoes there were three such membranes.

Dr. J. S. Porterfield cited virus isolations in Uganda and Israel which could be interpreted as denoting that minor antigenic changes were taking place quite rapidly at present. Dr. P. B. Stones advanced the hypothesis that if arbor viruses were evolved from mosquitoes one might expect to isolate viruses from male mosquitoes as well as from females, and reported the isolation of one virus from male mosquitoes collected in the British Cameroons. Dr. P. H. A. Sneath, arguing by analogy from bacteriophages, suggested that an arthropod-borne virus might obtain part of its genes from an insect, part from a bird, and part from a mammal.

The symposium raised important issues, some of which may be settled by further experimentation in the laboratory. It did not explain our freedom from infection with viruses of this group, but prompted the thought that certain undiagnosed " virus fevers " in this country may be due to unrecognised infections with arthropod-borne viruses.

RESECTION FOR PULMONARY TUBERCULOSIS IN THE ARMY

THE 500th resection for pulmonary tuberculosis was done at the Army Chest Centre at Hindhead on June 7. Of these operations, 137 were on Gurkhas and form part of an intensive effort, begun three years ago, to eliminate tuberculosis from the Brigade of Gurkhas.[1] Judging by the decline in the number of cases during the past year, this campaign is proving successful.

Normally, or course, pulmonary tuberculosis is nowadays treated by chemotherapy, and surgery is seldom needed. Outsiders may wonder therefore why the Army, with its relatively small population, should have so large a record of resections. In point of fact, since the first major thoracic operation was performed at the Army Chest Centre some seven years ago, a consistent policy has been followed, and resection has been limited to those segments or lobes (or even wedges) in which the disease has failed to clear after a reasonable period of chemotherapy. (Thus 16 Gurkhas have been sent back to Malaya without operation because the disease had resolved sufficiently to make surgery unnecessary.) But in deciding what is a " reasonable " period the facts of military life have had to be recognised. In the Services it is not always easy to provide the long-continued specialised aftercare sometimes needed for patients treated by chemotherapy alone. The man who remains under treatment may suffer from a stigma both in the mind of others and in his own. If there is only one lesion in his lung and it can be removed, the operation will restore his morale and help him to take his place again with renewed confidence in an organisation which, a few years ago, would have promptly discharged him as unfit. Morale in the soldier is constantly emphasised, and the Army Chest Centre has played a part in keeping it high.

Such a policy can stand only if the results of surgery seem to justify it. 2 patients died, but 1 of them was a man of 44 who had a massive myocardial infarction ten days after operation, and the only death associated with the operation was that of a man of 21 whose postoperative hæmorrhage may have been due to afibrinogenæmia. The incidence of complications, too, was remarkably low. It says much for the Army Medical Services that this specialised surgery should be done with such success under their auspices with the cooperation of civilian consultants.

1. *Lancet*, 1958, ii, 1053.

HOW MANY AUTOCLAVES?

ON page 643 of our present issue, Prof. Charles Wells and Dr. Francis Whitwell emphasise the remarkable output of a modern high-vacuum surgical steriliser if it is properly used. It is not yet appreciated how much more efficient is sterilisation by such instruments than by older less efficient sterilisers, especially when these were operated—as they often were—by methods which left something to be desired.[1–5] We may get a firm grip of this important matter by looking at the situation described by Wells and Whitwell. Before the sterilising process of a particular 650-bed hospital was modernised, the work was done in one large rectangular 72 c. ft. autoclave in which steam penetration was accomplished by downward displacement of air and the drawing of the usual preliminary partial vacuum. The weekly load averaged 1000 dressing-drums and 140 glove-drums. Every weekday the requirement of the hospital was for three loads of dressing-drums, each load requiring 160 minutes for its sterilising cycle, and one load of glove-drums, requiring 90 minutes. This work, together with the collecting and distributing of drums, required a team of two orderlies, one or other of whom worked daily from 7 A.M. to 9 P.M. with shorter hours at weekends. Observations reported from other hospitals [1–5] have now taught us that similar procedures seldom carried a good guarantee of sterility and that the risks accepted by deliberate under-treatment of gloves were not always free from tragic results. When modernisation was contemplated in the hospital referred to by Wells and Whitwell, forecasts of the capacity of the steriliser that would be required for the loads described ranged from 16 to 38 c. ft. In the event, the output of a modern high-pressure, high-vacuum

1. Bowie, J. H. *Pharm. J.* 1955, **174**, 473.
2. Howie, J. W., Timbury, M. C. *Lancet*, 1956, ii, 669.
3. M.R.C. Report, *ibid.* 1959, i, 425.
4. Nuffield Provincial Hospital Trust (1958).
5. *Lancet*, 1959, ii, 178.

autoclave of $3^1/_2$ c. ft. capacity came so near to meeting the needs of the hospital that the two orderlies, working in shifts from 7 A.M. to 10.30 P.M., were able to get through the work.

This remarkable demonstration, of course, is to be taken rather as a measure of increased efficiency than as a model of how these things should be arranged. For the type of hospital and work with which they were concerned, Wells and Whitwell think that an instrument of 9 or 10 c. ft. would be ideal in that it would allow a reasonable loading schedule, shorter shifts, and some expansion of work. All who are equally worried by present doubts about their sterilising methods and where the money is to be found for new apparatus may take heart from the facts disclosed. Obviously if the increased efficiency is of such an order that a steriliser of 10 c. ft. may do more work, and do it much more reliably, than one of 72 c. ft. the cost of safety is not to be nearly so great as at first glance it might appear to be. Moreover, as we recently remarked,[6] if hospitals will get together to rationalise their sterilising procedures in central sterile supply departments, still further advantages will accrue in the form of more highly skilled operators, better supervision, easier maintenance of sterilisers, and better arrangements for dealing with sudden emergencies. In general, big sterilisers, even of the modern high-vacuum, high-pressure type, are not to be recommended. The smaller-capacity instruments, of 25 c. ft. or less, obviate many difficulties of maintenance and make it far easier to get rid of the small amounts of air which remain even after a high vacuum has been drawn and whose displacement is essential in order to guarantee steam penetration into all parts of the load.

One further point in the valuable report of Wells and Whitwell deserves comment—namely, that rubber sheeting is not easily sterilised even in a highly efficient steriliser. This observation is in agreement with other unpublished experiences and it emphasises that the nature of rubber sheeting renders its sterilisation by steam in an autoclave a very difficult matter. In fact many supposedly sterile rubber sheets have proved to be as highly contaminated as the unsterile areas they were intended to cover. What is equally dangerous: a rubber sheet in a load may prevent adequate steam penetration to articles other than itself. We need to consider acceptable alternatives to rubber sheeting or more reliable methods of guaranteeing its sterility.

THE VERY DEAF CHILD

DURING the past fifteen years much progress has been made in training the hearing of the deaf child; yet the standard educational classification of deaf children in this country is still that laid down by the Board of Education's committee of inquiry in 1938. Though recent advances have made the whole classification out of date, many teachers of the deaf still regard it as sacrosanct and are horrified by any change from the recommendations of twenty-two years ago.[7] For example, the Association of Non Maintained Schools for the Deaf lately sent us a resolution which said:

"It has come to the notice of this Association that Grade III deaf children are being placed in Units for Partially Hearing Children, a move which is detrimental to the education of the severely deaf child. It is the unaminous opinion of this Association borne of long experience that all Grade III deaf children of any age should be placed in schools for the deaf."

The medical reader may ask "What are grade III deaf children?" The definition by the Board of Education's Committee was:

"The children in this Grade can hear and understand conversation at not more than 2 feet, if at all, though they may be able to hear vowels, with or without distinguishing between them, at distances greater than 2 feet. Their hearing loss is over 40 decibels (G.A.) or 60 decibels (P.T.A.) and may be total. Their speech and language, if any, are seriously defective, and, because of their loss of hearing, cannot be developed except by the methods of teaching applicable to deaf children who have not acquired speech and language naturally. This Grade does not include any children, no matter what their hearing loss, whose speech and language development are not seriously defective. The hearing of few children of this Grade can be improved by medical treatment, but many can be helped by the use of hearing aids."

The fallacy of this definition is the assumption that if the deaf child has not developed speech naturally by the time he is tested he never can and never will do so. Recent experience in many countries has shown that unbelievably small remnants of hearing can enable the child to learn speech through hearing if he is given the right help at the right time.[8–13] The first tests of hearing may show no comprehension of speech and only the ability to respond to vowel sounds and noises, but if auditory training is started, and the child is tested again after an interval, he will be found to have an apparent improvement in hearing. Even the pure-tone audiogram improves with training. This improvement is not a "cure" of the deafness; it is an improvement, through learning, in the perception and discrimination of sounds.

Failure to appreciate the apparent change in hearing which may follow training is the main reason why special schools are recommended as preferable. The value of such auditory training can be denied because its very success destroys the evidence of profound hearing loss. In contrast the non-auditory methods in special schools for the deaf preserve the hearing loss of the pupils unchanged.

The apparent change in hearing which is so dramatic in the deaf child is similar to the change that takes place every day in the hearing of the normal infant. The newborn infant cannot "hear and understand conversation" at 2 feet or any other distance. He has to learn the meaning of sounds, and he does this gradually during the first years of life—producing his first attempts at comprehensible speech after about a year of listening. Because his hearing is normal he can hear sounds easily and the learning process goes on without specific help—"spontaneously". The deaf infant depends on others to enable him to hear sounds loud enough and often enough for the learning process to take place: the sounds must be uttered into the ear, or (better still) he has a hearing-aid. Without this opportunity he will be dumb; with it he will develop speech, not so easily as the normally hearing infant, but by the same type of learning process. If the diagnosis is made early enough, in the first few months of life, and adequate auditory stimuli are provided, speech will develop almost "spontaneously" and subsequent admission to a school for the deaf is unthinkable.

6. *ibid.* Aug. 13, 1960, p. 353.
7. Board of Education: Report of the Committee of Inquiry into Problems relating to Children with Defective Hearing. H.M. Stationery Office, 1938.
8. Hardy, W. G., Pauls, M. D., Bordley, J. E. *Acta oto-laryng., Stockh.* 1951–52, **40**, 80.
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13. Whetnall, E. *ibid.* 1959, ii, 403.

Public Health

IN-SERVICE MENTAL-HEALTH TRAINING FOR HEALTH VISITORS

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THE Working Party on Health Visiting (1956) described health visitors as "general purpose family visitors" concerned largely with health education and social advice, and it recommended that they should undertake combined duties in public-health and medico-social work.

Edinburgh has about a hundred health visitors. The optimum number has not yet been recruited, and the present proportion is nearly one to every 4300 of the population. Progress has recently been made towards broadening the scope of health visitors' activities by combining duties in such a way that each is concerned with a whole range of services—antenatal, child welfare, school health, tuberculosis, and care of the aged—and thus becomes the general adviser to families in her own district.

The health visitor, being a registered general nurse with additional qualifications in midwifery and social medicine, may come in contact with a family through meeting the mother at an antenatal clinic, by regular visits to the home to see mother and baby, or through seeing the child at school. Contact at a later stage may arise in special circumstances—e.g., through tuberculosis or through one of the increasing number of old persons receiving supervision.

In addition general practitioners or hospital doctors may may refer patients to the health visitor. A health visitor is now attached to midwifery, pædiatric, and geriatric hospitals in Edinburgh to ensure, wherever necessary, adequate liaison and appropriate assistance in the rehabilitation of patients and in providing information on their home background. All these duties are performed in cooperation with the family doctor. Thus, inevitably, the health visitor comes in contact with psychiatric problems.

In view of the reorientation of the health visitors' field of work and the modern conception of community mental-health care, it was thought desirable to discover the extent to which mental-health care and aftercare could be included in health visitors' duties. It was necessary first to decide how the health visitor could best play her part without overlapping with other social workers. An important step seemed to be to increase contact between the local authority and hospital staffs, to foster mutual confidence and knowledge of each other's work. Information was sought on how best to give the health visitor more insight into the care and management of the mentally ill in the community. A basic knowledge of this work seemed likely to bring a more enlightened approach to prevention and ascertainment of mental breakdown at an early stage. The end result, it was hoped, would be a close integration of the services.

The experimental course was started in September, 1959. The hospital concerned in the training scheme is responsible for a population of about 170,000 people living in the southern and eastern parts of Edinburgh. Some thirty health visitors work in the homes and clinics in this area, and the majority were already doing combined duties. The health visitors (ten in number) who took part in the course were from the area immediately around the hospital, and each had about 400 families on her visiting-list. The superintendent of health visitors joined the course. A similar course for the other health visitors working in the hospital catchment area is planned to start shortly.

OUTLINE OF THE COURSE

The course, which was expected to continue for at least six months, comprised weekly lectures and discussions, with some clinical demonstrations and visits to various parts of the hospital. A preliminary aim was to make the health visitor feel at home with the psychiatrist's approach and the hospital "jargon". Small groups of health visitors attended the staff clinical conferences each week. In this way the health visitor would come to realise the various needs of the mental-hospital patient, and some cases would be allocated for aftercare. It was arranged that one of the health visitors would act as "liaison health visitor" and would attend two additional ward conferences each week to discuss whether potential referrals were practicable. Arrangements were made for health visitors and the senior psychiatric social worker to discuss problems arising in the supervision of patients in the community. Each health visitor spent a short period in the women's admission ward of the hospital to gain more complete insight into psychiatric nursing and treatment. Since the lecture-discussions were completed, there have been monthly meetings of the health visitors with the psychiatrist, the senior medical officer for mental-health services, and the hospital psychiatric social workers to discuss any administrative or clinical difficulties.

CONTENT OF THE COURSE

The course started with an introductory talk and discussion in the health department at which the senior medical officer for mental-health services outlined its purpose and plans. Afterwards there was a series of eight lectures by the psychiatrist, each lasting about forty minutes, which included history of the management of the mentally ill, psychological concepts, the treatment of recent admissions, rehabilitation of long-term patients, and administrative and medicolegal arrangements. Some stencilled lecture notes were provided. Each lecture was followed by a visit to a department of the hospital to illustrate the subject, and then a discussion took place over coffee with the psychiatric social workers and the matron or her deputy. The health visitors attended electroconvulsive-therapy sessions and the hospital case conferences in groups of two or three, on rota. After a talk by one of the psychiatric social workers on the functions and arrangements at the outpatients' social club a rota was arranged for the health visitors to attend in the evening.

By the ninth lecture, when the health visitors were initiated into the atmosphere and technical language of the hospital, it seemed opportune to invite the staff of the department of psychiatric social work and their students to join the meetings. The routine of the sessions was changed to an introduction and clinical demonstration of a particular psychiatric syndrome, followed by a discussion of its implications on the work of the health visitor and the psychiatric social worker. Copies of *Essentials of Case Work* (1957) were distributed, and this was discussed over the weeks with regard to the role of the health visitor in psychiatric cases.

The health visitor was now able to attend the wards as a nurse with at least some theoretical knowledge of psychiatry. She worked from 9 A.M. to 1 P.M. for six days, and found scope for her knowledge of physical illness as well as better orientation in mental nursing. Apart from her practical ward work, each health visitor spent about one and a half hours a week in the hospital.

During the course the psychiatrist accompanied each health visitor on one of her district rounds. The 4–6 cases visited were selected by the health visitor to represent a fair sample of her routine, and to include one or two with definite psychiatric bias. The visits also included child-welfare centres and school clinics. The psychiatrist thus became acquainted with the health visitor's routine and had the chance to observe her approach to patients. Later, the psychiatric social worker also accompanied the health visitor on her round to gain insight into her work.

RESULTS

As the course was exploratory and the experiment is still incomplete, the results are limited and the conclusions must be tentative. But the course has been judged helpful by both local-authority and hospital staff in view of the following achievements:

1. *Health visitors have gained insight into psychiatric states, diagnostic problems, management, and mental nursing.*

2. *Health visitors and psychiatric social workers have collaborated in the care of certain cases to their advantage and to the benefit of the patient.*

Exchange of information on psychological and physical aspects was of value to all. It was useful in some cases to arrange joint visits by psychiatric social workers and health visitors for a while before the health visitor continued alone.

3. *A number of psychiatric patients have been referred to health visitors for supervision and aftercare.*

During the first nine months of the scheme the health visiting service throughout Edinburgh undertook some supervision and investigation of 35 women and 12 men. These patients had been admitted to hospital recently or were under consideration for discharge. Very few were old people. The allocation of patients was not limited to members of the class. In about half the cases the work was undertaken in collaboration with the psychiatric social worker. The cases were selected by the doctors, psychiatric social workers, and liaison health visitor at the ward conferences. The health visitor for each case was then invited to the hospital to meet the patient and to get background and clinical information from the doctor in charge of the case and from the psychiatric social worker. In a few cases information only was contributed—e.g., from the knowledge of health visitors or others from local-authority departments who had dealt with the patient in the past. This information was often produced more efficiently by the liaison health visitor than any other way.

Clinically the largest number of patients referred had "depression", but patients with schizophrenic and paranoid illnesses responding to phenothiazine drugs were also included. Several patients had physical complications—e.g., diabetes, disseminated sclerosis and hemiplegia. 3 had concurrent pregnancies. In some cases the health visitor was already visiting the home because of young children or because the patient had tuberculosis.

4. *The health visitor has from time to time contributed relevant and valuable information at case conferences and discussions.*

5. *Administrative mechanisms have been worked out for appropriate referrals and information to be passed expeditiously between the services.*

As the role of the health visitor is at present controversial, and as it was planned to extend her function into the obvious territory of the psychiatric social worker, special care had to be taken to uphold the status of both professions. Referral of patients to health visitors only after discussion with the psychiatric social worker, and with direct responsibility to the doctor, satisfied the interprofessional needs and was at the same time practical from the clinical point of view.

The psychiatric social worker must have records which indicate changes in the patient's circumstances and problems. Difficulties of communication arise from the health visitor's mobility after her initial daily contact with headquarters at the health department. As the doctor deals with several social workers, lists are necessary to indicate the up-to-date distribution of the cases allocated to each worker. The liaison health visitor is a convenient person to transmit brief reports on behalf of her colleagues at the additional ward rounds which she attends.

6. *A greater understanding of the functions of each is fostered by collaboration between the public-health and hospital services.*

The liaison health visitor at the ward conferences, and the accompaniment of each health visitor on her round, have given the doctors a wider and clearer conception of the functions of local-authority departments, and have enabled both doctors and psychiatric social workers to achieve better working relations with them.

DISCUSSION

If the health visitor is to be a general family adviser, she must have a wider knowledge of the clinical and social problems related to mental illness. When the psychiatrist and psychiatric social worker accompanied the health visitors on visits several psychiatric cases were seen. The most frequent diagnoses were mental deficiency, anxiety states, and inadequate or neurotic psychopathy, but patients with senile and frankly psychotic states were also visited. In these circumstances a study by a health visitor of psychiatric patients and modern psychiatric treatment is not only desirable but necessary. Furthermore, closer association between health visitors and specialists in mental health is necessary if health visitors are to educate the community in mental health.

The health visitor must also be familiar with the less attractive aspects of the local mental hospital, and be able to differentiate fact from fantasy in ex-patients' reports. The health visitor can be invaluable in these days when mental hospitals still need ambassadors in the community.

The cases so far referred have been carefully selected and did not include difficult psychotic, psychopathic, or neurotic patients requiring special skills in management. Several cases had physical complications in which the nurses' previous training was relevant. Where visiting by both psychiatric social worker and health visitor was necessary, the closer liaison and understanding helped considerably.

One aim of the experimental course was to try to solve the problem of multiple family visiting. This was achieved even where both psychiatric social worker and health visitor visited the patient at first. In general it is desirable that any patient coming into a mental hospital who had been visited previously at home by a health visitor should, if possible, still be under her care for the psychiatric side.

The full history of new cases, however, should still be taken only by the psychiatric social worker, though, of course, health visitors should supplement the social investigations.

Another point is worth mentioning. Professional workers must appreciate that patients tend to classify them and give them what they regard as the appropriate information. Some may be irrationally anxious about the information to be passed on, or suspicious of visits made by health visitors on behalf of the mental-health services, unless the purpose of the visit is explained.

Finally, some health visitors may feel unable to accept the new and varied responsibilities of mental-health work, and others may not be suitable in temperament and personality, Hence both voluntary withdrawal from schemes such as this, and adequate selection procedures, must be arranged.

Our thanks are due to Dr. T. A. Munro, physician-superintendent, and Miss J. MacLeod, matron, the Royal Edinburgh Hospital, for their encouragement, helpful cooperation, and advice.

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Arsenical Haulm and Weed Killers

This is the last year in which arsenical haulm and weed killers will be used. The Ministry of Agriculture, Fisheries, and Food declares that farmers and their workers should be on the alert until the potato crop is safely stored and contaminated vegetable rubbish has been rendered harmless.

Certain precautions are required by law: workers preparing and applying the spray must wear protective clothing, and potato pickers must wear special protection if the crop is lifted within ten days of spraying.

Before spraying, warning notices should be erected at gates; unprotected persons should be deterred from entering the fields. There is a serious risk to livestock if fences are not stock-proof.

Serious accidents have been caused by water-supplies becoming contaminated during preparation of the spray. Spray tanks should always be filled in the field where they are to be used, and great care is needed to prevent spilling. When cleaning the machinery, attention must be paid to safe disposal of the washings. Care is also needed to ensure safe storage of full containers of the concentrate. Empty containers should be punctured to prevent further use and be burned, buried, or otherwise disposed of safely.

African Horse Sickness

The epizootic of this disease which is now in progress in the Near and Middle East[1] has spread to Cyprus. At the weekend [2] 30 to 40 animals were reported to have died. Cypriot officials have asked the United Nations Food and Agriculture Organisation in Rome to send preventive vaccine.

1. *Lancet*, July 9, 1960, p. 84.
2. *Times*, Sept. 12, 1960.

Special Articles

A SMALL AUTOCLAVE IN A LARGE HOSPITAL *

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Broadgreen is a general hospital of about 650 beds. It includes a maternity unit of 90 beds, about 200 general surgical and gynæcological beds, the regional thoracic unit of 100 beds, about 90 orthopædic beds, and a small faciomaxillary unit. There are five busy operating-theatres.

The Old Autoclave †

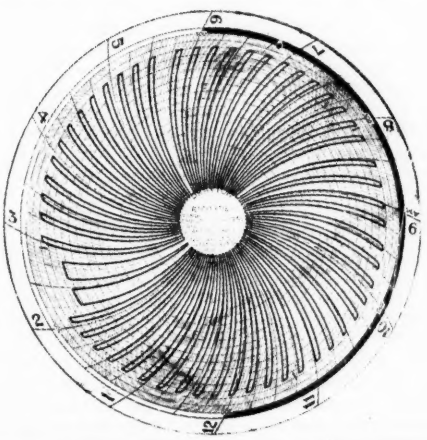
Until November, 1959, all the hospital autoclaving of dressings, gowns, towels, swabs, and gloves was done in one large rectangular downdraught-displacement autoclave of 72 c. ft. capacity, drawing the usual partial vacuum. The weekly load averaged 1000 dressing drums and 140 glove drums. Every weekday three loads of dressing drums, each lasting 160 minutes, and one load of glove drums, lasting 90 minutes were required, The autoclave was operated by one member of a team of two orderlies working from 7 A.M. to 9 P.M. The duties of this team also included collecting and distributing drums. At weekends, when there were fewer loads, shorter hours were worked.

In the summer of 1959 it was decided to remove the autoclaving from a room in the theatre suite to a separate department, and to consider replacing the large autoclave by a smaller high-speed high-vacuum model. Five manufacturers of such equipment were consulted, given the weekly drum turnover, and asked what size of machine would be needed. Their replies varied from 16 to 38 c. ft.

The New Autoclave

In November, 1959, a local manufacturer lent the hospital the prototype of a high-speed high-vacuum cylindrical autoclave of $3^1/_2$ c. ft. capacity. A number of minor modifications were made by the manufacturer, and for the last three months the instrument has given continuous service at a phenomenal rate of turnover.

The machine has two fully automatic cycles—one for dress-



An untouched reproduction of a typical 12-hour time/temperature recorder chart, showing the total number of complete cycles between 8.0 a.m. amd 8.0 p.m. (fifty-three dressing loads and two glove loads)

A larger-scale continuous strip record could be more easily read with such short runs.

* A report to the Medical Research Council Working Party on Pressure-Steam-Sterilisers.

† "Autoclave" is not a strictly accurate term but is convenient and well understood.

ings and one for gloves. It can also be worked by hand, although it has not been used in this way. The dressing cycle is:

1. About 3 minutes to draw prevacuum down to 0·8 in. (20 mm.) positive pressure—i.e., 29·2 "inches of vacuum" at 30 in. Hg atmospheric pressure (holding-time nil).

2. About 1 minute to attain 276°F (135°C) at a steam pressure of 32 lb. per sq. in. (holding-time 3 minutes).

3. About 2 minutes to draw postvacuum 1·6 in. (40 mm.) Hg (holding-time nil).

4. About $^1/_2$ minute to break the vacuum.

Approximate total for cycle = $9^1/_2$ minutes.

An absolute-pressure switch is fitted to ensure that the cycle cannot change until the correct degree of vacuum is obtained.

An integrator is fitted which maintains a predetermined relation between time and temperature throughout the sterilising part of the cycle. Opinions differ about the need for this rather expensive piece of apparatus. Under ideal conditions the optimum temperature is quickly reached, and the holding-time can then be simply measured. If the main steam supply is variable, however, and especially if the chamber is large, the predetermined pressure and temperature may be reached more slowly. In these circumstances the integrator makes allowance for the sterilisation effected by the steam as it is building up to the predetermined pressure and temperature. In addition, the integrator compensates for the small variations in pressure that may arise if the main steam supply is less than perfect. In this particular autoclave, and at this particular hospital, the integrator is probably unnecessary, but it is a standard part of the 'Drayton' control system.

The glove cycle is the same as the dressing cycle, except that a steam pressure of 17 lb. per sq. in. (251°F or 121°C) is held for 15 minutes.

Our original aim was merely to test the efficiency of the autoclave using thermocouples, Browne's tubes, and spore papers, for differently packed drums during both cycles. But, the early results were so satisfactory that in addition we have tested the mechanical reliability of the machine by overusing it. We have, at the same time, gained valuable and rather surprising information about the possible turnover with a chamber as small as $3^1/_2$ cu. ft.

THE TESTS

Thermocouple tests gave results within the chamber identical with those recorded by the machine.

Browne's Tubes, type 1 (black spot), as is already known, do not change to a true green with high-speed processes because there is not long enough for the chemical reaction to occur. Browne's tube, type 2 (yellow spot), is now known to be suitable for use in high-vacuum high-pressure sterilisers for both gloves and dressings. One tube was put into at least one drum of each load, and a tube was also put into each large chest-unit drum. The results were satisfactory except for occasional large chest-unit drums containing heavy rubber sheets.

Spore tests were made fortnightly on dressing and drum cycles using *Bacillus stearothermophilus*. All spores were killed except those in one large chest-unit drum containing rubber sheets.

Moisture.—Only occasional large drums from the chest unit, with the rubber sheets mentioned above, failed to dry completely.

Mechanical reliability and capacity.—For over 3 months this instrument has daily autoclaved about 160 dressing drums (in about fifty loads) and 24 glove drums (in three loads). It is managed, in shifts from 7.0 A.M. to 10.30 P.M. by one operator of two, whose duties include collecting and delivering drums in the hospital, as before.

Thus, this one small machine is handling 90% of the total hospital work, although the operator's hours have needed to be increased by 10%. Obviously, this rate of work is undesirable, probably overstraining the machine and certainly overworking the operator who has to load and unload five times an hour, but it proves conclusively the enormous capacity of the new machine.

CONCLUSIONS

1. We find this machine very satisfactory.

2. Cylindrical autoclaves have definite mechanical and cost advantages over rectangular ones. We do not concur with those who think, that from the user's standpoint, a rectangular chamber is so far preferable as to outweigh the undoubted mechanical and cost advantages.

3. A suitable size of autoclave of this type, for this hospital and allowing for some expansion of work, would be 9 or 10 c. ft. This would reduce the loading and unloading to four times an hour, and allow the operators to work shorter shifts.

4. We are not convinced that a separate glove cycle is necessary. We have evidence which suggests that gloves autoclaved in the dressing cycle last quite as long as those done in the glove cycle. Further experiments are needed, and these are being made.

5. Large drums are undesirable, and we have shown that large rubber sheets are relatively difficult to sterilise. For many reasons, including the efficient packing of the chamber, individual packs should be brought into routine use in place of drums.

6. Large rubber sheets should not be used.

We are indebted for the fullest possible cooperation and assistance to the Liverpool Regional Hospital Board and the hospital management committee; and to Messrs. Henry Wilson, of Cornhill Works, Kirkby, Liverpool, who made and supplied the autoclave.

Conferences

NEPHROLOGY

THE 1st International Congress of Nephrology was held at Evian from Sept. 1 to 4.

Tubular Function

It was suitable that H. WIRZ should give the first paper, for much of the subsequent work that was presented confirmed and elaborated the brilliant hypothesis which he, together with HARGITAY and KUHN, first proposed about ten years ago. It now seems a generally accepted view that the counter-current of fluid in the medulla is involved in the mechanism of urine concentration. R. W. BERLINER and others, including C. W. GOTTSCHALK, W. E. LASSITER, M. MYLLE, K. J. ULLRICH, B. SCHMIDT-NIELSEN, G. PEHLING, and R. O'DELL, presented evidence which supported the counter-current hypothesis. They have extended Wirz's original observation and shown that the fluid at the tip of the loop of Henle remains hypertonic when the urine is hypotonic; that urea is reabsorbed from the collecting ducts during antidiuresis; and that water is reabsorbed throughout the whole length of the nephron including the loop of Henle, whether the final urine is hypotonic or hypertonic. Perhaps the neatest confirmation of the countercurrent hypothesis was the demonstration by F. MOREL and M. GUINNEBAULT that if radioactive sodium and tritiated water are injected simultaneously into the renal artery, and the kidney removed a minute later, the sodium is seen to be trapped in the medulla, there being little or none in the cortex, whereas the tritiated water is only present in the cortex.

C. W. GOTTSCHALK et al. also found that during an osmotic diuresis the fluid obtained from the proximal tubule had a fluid-to-plasma sodium concentration ratio of approximately 0·75—additional evidence for active sodium reabsorption in the proximal tubule. There was general agreement, in accordance with the findings of E. M. DARMADY and his colleagues with labelled vasopressin, that antidiuretic hormone (A.D.H.) must act on the distal and collecting tubules and that it probably changes the permeability of the tubule wall. There was some discussion whether, in addition, A.D.H. might not alter the rate of blood-flow through the medulla and so influence urine concentration. L. S. LILIENFIELD and H. C. MANGAZINI, however, using one technique for measuring medullary blood-flow, and K. KRAMER and K. J. ULLRICH using another, obtained completely contradictory results when estimating the change in blood-flow when urine concentration changes. It was pleasant to hear that the two sets of workers were now working together to try to resolve their differences. J. B. LONGLEY, M. S. BURSTONE, N. A. LASSEN, W. G. BANFIELD, and D. C. BRINDLEY showed that the afferent limb of the vasa recta is much thicker than the efferent limb. They were able to distinguish the afferent limb because of its content of esterase which allows it to be stained differently from surrounding structures.

Stop-flow Technique

One morning was spent discussing the stop-flow technique of R. L. MALVIN, W. S. WILDE, and SULLIVAN—a manœuvre that Pitts has called the "poor man's micropuncture". E. ULLMAN and F. MOREL both presented evidence that glomerular filtration continued throughout the time that the ureter was obstructed. It was generally agreed, therefore, that this technique can perhaps give some information about distal tubular function but that it is an unsafe guide to proximal tubular function. The results obtained on fluid considered to come from the distal and collecting tubules are in keeping with evidence obtained by micropuncture. The neatest variation on the stop flow technique was described by D. E. OKEN. He places fluids of known composition in selected parts of a nephron with a micropipette, the fluid being prevented from moving away from this site by being wedged between two drops of oil. After varying intervals the fluid is removed and its content analysed. His evidence confirmed that of Morel obtained by ordinary micropuncture techniques that potassium appears to be moved passively into the lumen of the tubule by passing along an electric potential gradient.

Potassium Metabolism

S. W. STANBURY gave a masterly review of the relation of the kidney to potassium metabolism. He pointed out that the intracellular content of potassium is an important factor in the kidney's ability to excrete potassium, and that, as the administration of potassium to sodium-deficient patients increases sodium excretion, potassium can probably interfere with sodium reabsorption, perhaps in the proximal tubule. He listed the conditions in which excessive potassium excretion occurs and underlined the work of J. W. MILLS, S. THOMAS, and K. S. WILLIAMSON who have found that aldosterone increases potassium excretion while decreasing hydrogen-ion excretion, whereas cortisol increases potassium excretion without changing hydrogen-ion excretion. F. C. BARTTER discussed the various mechanisms known to influence the secretion of aldosterone, including hæmodynamic factors, total body-potassium, corticotrophin, and changes in the electrolyte concentration of the blood perfusing the adrenals. In addition he had recently found that intracarotid infusion of potassium could also cause a rise in aldosterone secretion, though the same amount given intravenously had no effect. Hypophysectomy abolished this change. He then described what subsequent speakers called Bartter's syndrome. He had only one case—a boy with a renal leak of potassium associated with increased aldosterone secretion and adrenal hyperplasia. Renal biopsy showed gross hypertrophy of the juxtaglomerular apparatus, which in many glomeruli had invaded and obliterated the glomeruli. The implication that some substance elaborated by the juxtaglomerular apparatus might have stimulated aldosterone secretion was not mentioned, though it hung heavily in the air. It was supported later, when J. LARAGH demonstrated that an infusion of angiotonin raised aldosterone secretion. It seemed as if once again a patient had presented an invaluable clue.

Aldosterone Secretion

A. F. MULLER pointed out that the upright posture increased aldosterone secretion, and that the usual diurnal rhythm of aldosterone secretion, therefore, was often abolished if the person stayed in bed. He discussed what is now known as the "escape" mechanism to aldosterone—that is, the ability of a healthy person to regulate urinary sodium excretion and maintain a steady sodium balance while being given a constant infusion of aldosterone. This "escape" mechanism cannot be demonstrated in patients with hypopituitarism or œdema. He emphasised that the increased aldosterone excretion in œdematous patients is perhaps only a small factor contributing to the œdema. His results showed that there was no relationship between the increase in sodium excretion which might follow the administration of spiralactone and the rate of aldosterone secretion immediately preceding its administration. He confirmed Shaldon, McLaren, and Sherlock's findings that a most effective way to produce diuresis in patients who are resistant to the usual methods is to give a combination of chlorothiazide and spirolactone.

Acid Urine

W. B. SCHWARTZ discussed the ability of the kidney to form an acid urine and the changes in the rate of urinary excretion of titratable acid, ammonia, and bicarbonate in chronic renal failure and renal tubular acidosis. His main point—that a bicarbonate leak was a primary cause of the systemic acidosis in both conditions—was severely challenged by D. W. SELDIN, who pointed out that, if for some reason there is a primary impairment of the ability to acidify the urine, bicarbonate excretion must continue, and that the leak of bicarbonate in such a circumstance is not evidence of impaired capacity to reabsorb bicarbonate. This objection to Schwartz's conclusions applied particularly to patients with renal tubular acidosis.

The Kidney in "Shock"

From this discussion it was clear that the word "shock" means as little in the rest of the world as it does in this country and that semantic clarity would best be served if it ceased to be used. P. VASSALLI described a "shock kidney" as acute renal failure due to acute reduction in renal blood-flow whether or not there was any clinical evidence of "shock"; whereas M. LEGRAIN's description was acute renal failure accompanied by an undefined "vascular collapse". One outstanding fact emerged: it was agreed that once acute renal failure was established the reduction in renal blood-flow down to approximately a third of normal which was usually found (O. MUNCK) could not be the cause of the persistent anuria. Munck also pointed out that there is at the moment no evidence as to what takes place during the initial phase of acute renal failure, and that, though it seems reasonable to suppose that there is usually an intense renal vasoconstriction, no measurements have been made at this time. There was a brief discussion of treatment by dialysis, under the chairmanship of J. P. MERRILL. It was agreed that it was better for the patient to be dialysed at short intervals. P. E. TESCHAN dialyses every day but avoids repeated cut-downs by inserting plastic cannulæ into the radial artery and forearm vein which he leaves in situ until the end of treatment. B. H. SCRIBNER dialyses continuously throughout the twenty-four hours. It was also agreed that it is better not to heparinise the patient but instead to heparinise the blood as it enters the dialyser and then to give protamine to the blood as it leaves the dialyser. There was much discussion and no agreement as to whether cases of chronic renal failure

should be dialysed. C. BRUN and J. P. MERRILL thought it unwise, whereas N. ALWALL did not think that a generalisation was possible. Finally, those at present in charge of dialysing centres thought that their number should be limited, preferably to the number at present in existence. Surprisingly, the well-known objections to this recurrent ladder-lifting syndrome were not voiced.

Renal Transplantation

In this exciting session J. P. MERRILL and J. HAMBURGER described the successful transplantation of kidneys from donors to recipients who were not identical twins. Both speakers described how they first irradiated the recipients with approximately 450r from a cobalt bomb, to depress immunological processes. Hamburger then placed the patient in a bacteria-free room, and the transplantation was performed under hypothermia on the day after the end of the irradiation. Merrill had one patient alive after a year with good renal function and no proteinuria, though six months after the operation proteinuria had begun to appear. This ceased after a further course of irradiation. Hamburger had had two successful cases, one for one year and the other for six months; the latter a girl of 21 had recently married. The transplant was most likely to be successful if the donor was a close relative of the recipient. Later P. P. LAMBERT, and R. KUSS, M. LEGRAIN, and G. MATHÉ described other cases.

Other Topics

R. L. VERNIER demonstrated that the glomerular foot processes of dogs will become smudged after the intravenous administration of dog serum-protein, if it is given in such large amounts that proteinuria is induced. The foot processes returned to normal when protein administration was discontinued. This is a fairly convincing demonstration that the smudging of the foot processes in the nephrotic syndrome is probably secondary to the proteinuria.

T. D. ULLMAN showed that the antidiuretic effect of vasopressin during water diuresis was influenced by the pH of the urine and that during the formation of an alkaline urine there was relative insensitivity to exogenous vasopressin. It was pointed out that though there is as yet no explanation for this unexpected finding it is in line with Nutbourne and de Wardener's observation that hydrogen-ion excretion is depressed by a water diuresis.

Finally, there was Y. J. KATZ and R. S. MOORE's demonstration that the increase in white-cell excretion which follows an intravenous injection of a pyrogen in chronic pyelonephritis (Pears and Houghton) can also be obtained by the intravenous administration of 20 mg. of prednisone phosphate.

An International Association

During the congress it was decided to form an International Association of those interested in the kidney, and Prof. J. HAMBURGER was unanimously elected its first president. It was proposed that there should be another international congress in three years, and an invitation from Dr. Jan Brod to come to Prague was accepted.

H. E. DE WARDENER.

CLINICAL ENZYMOLOGY

The 6th International Congress of Internal Medicine, held at Basle on Aug. 24–27, included a day devoted to Enzyme Regulations in the Clinic.

H. THEORELL (Stockholm) surveyed the various modes of enzyme action, taking catalases, cytochromes, and dehydrogenases as typical examples. It was important to elucidate the exact mode of action of an enzyme before using it as an analytical tool. When this had been done, then enzyme measurements were as accurate as any other microchemical technique.

C. H. GRAY (London) discussed the difficulties of measuring enzymes in body-fluids. The ability to read a galvanometer needle with an error of less than 0·1% did not mean that the final calculated result had the same accuracy. Clinical enzymology often produced results of relative significance only, and in the congenital abnormalities there was need for absolute values.

The relation between genes and enzymes was reviewed by E. HADORN (Zürich), who discussed the "one gene—one enzyme" hypothesis and the possibility that a single gene may control several enzymes or an enzyme with multiple functions.

The functions and metabolism of organic phosphate compounds in heart-muscle were described by A. FLECKENSTEIN (Freiburg); and R. L. BING (St. Louis) gave a stimulating account of enzyme changes in cardiac metabolism. The heart contained enzyme systems capable of utilising all the foodstuffs circulating in the blood but appeared to preferentially catabolise esterified fatty acids, particularly esters of oleic acid. Studies on cardiac biopsy samples in the dog showed that tachycardia and ventricular fibrillation resulted in temporary increase in active phosphorylase together with accumulation of lactic acid.

J. V. TAGGART (New York) considered the role of enzymes in renal metabolism, particularly with respect to the transport of substances across the tubular epithelium. The exact location of the various enzymes in different segments of the nephron and the identification of the components of the transport mechanisms were the most challenging problems in current research.

L. VILLA (Milan) classified hepatic enzymes as primary, secondary, and accessory. C. J. WATSON (Minneapolis) described bilirubin metabolism and discussed in detail the extrahepatic conjugation of bilirubin. Even the severely damaged liver could both conjugate bilirubin and synthesise dihydroxy bile acids. M. J. H. SMITH (London) reviewed the use of blood-enzyme determinations in liver disease and concluded that it was not possible to distinguish specific patterns of blood-enzyme abnormalities for each hepatic disorder. But serial estimations of transaminases and of other enzyme activities could give valuable help both in the diagnosis and in the assessment of the course and prognosis of particular liver diseases.

The use of enzyme measurements in liver disease was discussed at length by a panel which included F. WROBLEWSKI (New York), F. SCHMIDT (Kassel), and D. ALLDIS (London). The heterogeneity of serum enzymes, the misconception that necrosis of the liver accounts for raised blood-enzyme activities, and the significance of serum-alkaline-phosphatase activities provoked vigorous debate.

A. VANNOTTI (Lausanne) dealt with the enzymes present in the various cellular elements of the blood and with the effects of inflammation and hormone treatments on the enzyme patterns in leucocytes.

J. B. STANBURY (Boston) distinguished five types of congenital hypothyroidism as inherited enzyme defects concerned with different stages in either the synthesis or the metabolism of the thyroid hormone. One of these syndromes—that caused by a deficiency of a dehalogenase enzyme—was described in detail by A. QUERIDO (Leiden). The primary defect appeared to be inability to dehalogenate iodotyrosine compounds, which led to increased urinary excretion of organically bound iodine and lack of inorganic iodine for recirculation and incorporation into thyroglobulin. The ultimate effect was a conditioned iodine deficiency causing decreased thyroxine synthesis.

The discussions on clinical enzymology are to be published as a separate volume of the Congress proceedings.

In England Now

A Running Commentary by Peripatetic Correspondents

ONE view of members of hospital boards of management is that they are high-minded men and women, fired with enthusiasm for the public weal and anxious to sacrifice time and leisure for suffering humanity. Another is that they are an ill-chosen collection of long-winded ninnies who would find difficulty in organising a game of ludo. My own attitude bears a relation to the date of the last board meeting and how fresh in my mind is the dissertation by Baillie MacSpittle on the incomparable superiority of wax polish over synthetic for the dining-room floor (his homily being interrupted by Lady Bluebell's reminiscences of the ballroom at the Hall in her father's time, the demands of Mr. Smithkins, M.B.E., trade unionist, for enlightenment on the demarcation dispute between Matron and Secretary, and General Roderick Philabeg's contention that all that is needed is damned elbow-grease), while my cherished and logically presented plan for the urgently needed treatment-room is dismissed out of hand. I suppose the truth lies somewhere between the two extremes. But at board meetings I often find myself repeating under my breath the well-known remark that a camel is a horse planned by a committee.

* * *

A short time ago, somewhat unwillingly, I accepted sound advice to undergo a major surgical procedure.

I was admitted to an extremely pleasant single room, complete with wireless and television, in a well-known women's hospital. From this moment I was regarded as potential medical dynamite. Not only was I a woman doctor, but I was also married to a doctor and all felt that the most unusual complications were likely to develop. The time of my operation was delayed so that ample blood should be available as my hæmoglobin was found to be low. In fact, from my point of view the operation and anæsthetic could not have been more perfect. The postoperative period passed in a delicious haze of pethidine with remarkably little discomfort. I was quickly mobile and felt incredibly fit. The time came for the removal of my clips by the surgeon himself. The result was a stunningly beautiful scar; sister was in raptures. The final accolade came when the house-surgeon diffidently asked if he might view the masterpiece as its fame had spread. Nevertheless sister was pleased to see me go. She admonished me before her day off not to do anything rash—she felt her good luck could not last. And there was an audible sigh of relief all round when on the twelfth day I successfully took myself home.

For my part I enjoyed my surgical experience far more than I thought possible and was extremely happy except for one thing, the hardness of the mattress. It was gorgeous to go to bed at home and relax in comfort. Why, I wonder, do hard hair mattresses still linger in modern hospitals?

* * *

Probably not many of us bother ourselves with such erstwhile issues as whether a viscount's half-brother should precede into dinner a duke's cousin once removed. What does matter, however, are the problems of etiquette which arise on the London Underground.

The lift presents no great problems; it is commonplace that the lady goes ahead of gentlemen—tradition demands it and there is the further point that the man is better placed to prise the wandering stiletto heel from the groove in which the gates run. And, of course, the man must take the risk of premature closure and entrapment. Then he must remove his hat, put out his cigarette, and protect the lady from asphyxiation as far as possible. Escalators are trickier. Notwithstanding the high-heel hazard, he should go first on the way down, providing a "soft-landing" as it were, and for the same reason second on the way up. The extent to which one should conduct oneself thus with regard to *all* ladies, apart from one's travelling companions, is open to question. Strict observance of etiquette is likely to prolong travelling-time unduly, and might even be misconstrued.

Purchase of the tickets presents no special difficulties, but entry to the train is another matter, and this depends entirely on population density. The gentleman must judge the ease with which entry to a crowded train may be forced and go in first if necessary with his umbrella so as to prise open a space of sufficient size. Two can seldom walk side by side down the passages—and here we must be quite firm. The lady must *always* go first, even though by following the green light for Victoria she may inadvertently land you at London Bridge.

* * *

I seem to remember that, some years ago, Dickson Wright described the National Health Service as wailing and nationalisation of teeth. Is bruxism an occupational disease of medical practitioners?

* * *

The professional doctor's friend opens her attack subtly. "We are looking for a doctor with young children himself," she says as the voices of my three children invade the wire from the upstairs extension. "Yours sounds a family home." The professional touch develops later. "We were such good friends with our previous doctor—he almost lived at our house—I remember one Christmas Eve—he used to stay for hours—he was marvellous with the children—the weekend Aunt Sara came we called him three times—he never minded—we're hopeless about the surgery—I always seemed to be ringing his home at half-past ten." She and her family are most likeable folk and the propaganda works. Two late evening calls and I find myself thinking, "Why can't I be their best friend like Harvey Doolittle? How could he do it? Did he enjoy the situation, had he no real friends, or had he, like me, tried too hard and succeeded?" "I don't understand these people always sending for a doctor; it's different among friends, otherwise I wouldn't dream of sending till we were desperate—except with children." Desperately I look round for fresh interests. Harvey seemed to be a Leonardo. He was marvellous with old wireless sets, he founded a boys' club, he was a churchwarden. Alas, my glaring defects do not count against me, for I am a collector's piece, indispensable to the smooth running of their home. Soon they are embossed in the visiting-list like their address on my prescription pad. At last they move on. Their new home is conveniently near the new surgery. "We are sure we are going to like him."

* * *

East-West trade note.—We took our eleven-year-old to hear the Leningrad Symphony Orchestra. He disappeared during the interval and came back without his tie (a hunting Stuart tartan). He had exchanged it for two Sputnik badges, a 20-kopek piece, 10 autographs, and, thrown in, a kiss from the trumpeter.

* * *

SE TAIRE C'EST PLAIRE

Among the rarest
(Seamus said)
Of all the family joules
Was formerly a hard-boiled erg
And on its sleek and shining shell
Was writ "O Man!
Think'st thou
T'evade the circumambient here and now?
Dost dream
Of some seductive but fallacious scheme—
Of some eternal effort-saving notion?
No! Accept the yoke
Be meek
Fall not into temptation
Do not seek
Perpetual motion but perpetual motivation!"
Well
Of course the thing is sold
But it was pretty to behold.

Letters to the Editor

ONE FORCES' MEDICAL SERVICE?

SIR,—The fact that I was arrested as a spy on entering a British front-line trench on the Pilckem Ridge in the first world war does not deter me from leaving the underground council chamber of the British Medical Association to make a sortie into what I suspect from reading your annotation of Aug. 13 to be a somewhat hastily prepared position.

You note (with glee?) that the Select Committee on Estimates in their fourth report criticised the Service Departments as "disappointingly inflexible" and consider that the latest observations of the Ministers concerned "will do little to alter the Committee's view", implying that any "stagnation of trench conflict" which may ensue will primarily be due to the Service departments and the Ministry of Defence.

But you do not note, as did the B.M.A. council with the advice of its Armed Forces Committee, any of the following significant points regarding the findings of the Select Committee:

1. That the main recommendation for integration was not supported by the weight of evidence. Nearly all the evidence given to it from all sources—independent and civilian as well as Service and official—was either against it or did not support it.

The conclusion upon which it was based—"The objections to integration formulated by the Waverley Committee have in large part been weakened or invalidated by subsequent events, and the inauguration of the Canadian scheme"—was unsound. The only changes we know of are those beneficial ones which have followed the adoption of some of the Waverley Committee's recommendations. The only witness heard by the Select Committee who was also a member of the Waverley Committee was Sir Arthur Porritt. He stated in evidence: "I think—and I still feel as I did then, perhaps even more so—that it would be a great pity from a recruitment point of view, from the medical angle, that they should be amalgamated", and, again: "I believe most of the things we want to achieve can be effected by increased co-ordination and not amalgamation, considering the traditions behind the Services."

2. The Mond Weir Committee in 1923, the Government in 1946–48, and the Waverley Committee in 1955 considered that integration would be unlikely to show substantial economies or increased efficiency, and would be likely to affect adversely medical recruitment.

No evidence is given of any economies or of greater efficiency which would arise from integration, nor does the Select Committee specify how these things will be obtained.

It is not surprising, of course, that no evidence was given of these things resulting from the Canadian scheme, because that was inaugurated only 12 days before the Select Committee began to hear evidence!

3. There appears no justification on present evidence for throwing aside our traditional freedom of choice for young doctors to make a career in a Service to which they feel particularly attracted.

In the incident referred to in the first paragraph, I was sent back to battalion headquarters between fixed bayonets and given lunch in the mess as part of a test. Should you wish to test any of the above points, I should be happy to submit in a similar way in your headquarters.

REGINALD STANBRIDGE
Oxshott, Surrey. Chairman, Armed Forces Committee, B.M.A.

*** After the late war, we were demanding integration [1] with as much vigour as Air Vice-Marshal Stanbridge opposes it. Our comment on the Select Committee's report did justice to the objections,[2] but we still want to see the Services brought closer together.—ED. L.

1. *Lancet*, 1946, ii, 421, 523; 1947, i, 373; 1947, ii, 799.

ORNITHOSIS AND RAILWAY GUARDS

SIR,—The editor of the *Racing Pigeon* has now twice asked (July 16, Aug. 27) for evidence of ornithosis infections in humans resulting from racing-pigeons.

In 1948 we found evidence of ornithosis infection in the family of a pigeon-fancier, and we started serological investigations of racing-pigeons and other domestic pigeons. Soon we found a high percentage of serologically positive reactions with ornithosis antigen in racing-pigeons and a low percentage of positive reactions in any other type of domestic pigeon. Subsequently, Winsser [3] isolated the virus from pigeons which had been a source of infection. We have since examined more than two thousand serum samples of pigeons and never found a group of racing-pigeons in which less than 30% showed serological evidence of infection; from many of these pigeons virus isolation was relatively easy. We did find some groups of pigeons without evidence of infection, but none of these were racing-pigeons.

It should be emphasised that ornithosis virus has a very low pathogenicity for pigeons, and that birds which are apparently in a very healthy condition excrete this virus and are consequently infective to their fellow-travellers in railway vans, to their caretakers there, and to their owner and his family at home. As racing-pigeons frequently travel together, sometimes for days, in a relatively small space, it is obvious that few of them could hope to escape infection.

The infectivity and virulence of this pigeon-ornithosis-virus for man are also very low: although most pigeon-fanciers have positive complement-fixation tests with ornithosis antigen, some of them may have negative reactions even if their loft is heavily infected and virus is readily isolated from the birds. Of 843 ornithosis patients diagnosed in the Netherlands since 1948, 270 had had contact with pigeons (mainly racing-pigeons); only 80 of these were women.

Since 1950 clinicians in this country have been increasingly aware of the possibility of ornithosis in cases of atypical pneumonia, and now 4000–5000 serum samples from these patients are examined annually; we feel that perhaps half the patients seriously ill with ornithosis with pigeons as the source of infection are diagnosed as such; the annual average is about 25. As there are about three hundred thousand organised racing-pigeon fanciers in the Netherlands, the risk of infection is obviously very small. This risk should therefore not be exaggerated; but it is impossible to deny it as Mr. Osman does. Furthermore, there is an obvious difference between racing-pigeons and other domestic pigeons in that the former are certainly more heavily infected than the latter. I think that any British virologist who would care to examine the serum of racing-pigeons for evidence of ornithosis infection would get the same results we did.

Central Institute for Ornithosis Research of the Netherlands Public Health Service, Amsterdam. F. DEKKING.

UNITS

SIR,—Dr. Eaton's plea last week for uniformity in the use of units reminds me of a lecture on corrosion by the late Dr. W. E. Gibbs, Ramsay professor of chemical engineering at University College, London. Quoting corrosion-rates expressed in milligrammes per square foot per day, Professor Gibbs added: "I apologise, gentlemen, for these bastard units. But what else can one expect from the union of chemistry with engineering?"

Newcastle upon Tyne. F. H. BELL.

2. *ibid.* 1959, ii, 336.
3. Winsser, J., Dekking, F., en Stol, H. J. *Tijdschr. Diergeneesk*, 1949, **74**, 423.

OUR POOR THAMES

SIR,—Dr. Mackenzie-Wintle writes in your issue of Sept. 10: "I have spoken to many doctors, but I have yet to find one who can quote me a single case of typhoid, poliomyelitis, or even Weil's disease which could reasonably be presumed to have its origin in the ingestion of river water."

If he means by this that leptospirosis is not contracted by ingestion he may well be right, but if he intends to imply that the Thames water does not convey the infection then I believe him to be quite mistaken. In the past few years I have had at least a score of cases in men and boys following bathing or fishing in the river or its tributaries. Most cases were mild—far removed from the usual textbook descriptions—and might well have escaped detection had the condition not been suspected, and the appropriate investigations carried out.

Certainly in this part of the Thames Valley leptospirosis must be seriously considered in the differential diagnosis of hepatitis and/or meningitis. Renal lesions, while present, are rarely obtrusive.

South Middlesex Hospital, Isleworth. G. E. BREEN.

SIR,—It is without surprise that we learn from Mr. Basil Jarvis (Sept. 3) and Dr. Mackenzie-Wintle that the Thames is heavily polluted with fæces much nearer to its source than Staines.

Dr. Mackenzie-Wintle's advice that "the healthful effects of [river] bathing very far outweigh any risk involved" we feel is an astonishing statement to come from anyone having specialised knowledge of waterborne diseases. A little over a hundred years ago critics of Dr. Snow must have made similar statements when he pointed out that the cholera epidemic that raged in Soho was associated with water from the Broad Street pump.

We would like to point out that all or practically all bathers swallow some water while swimming; many swallow a considerable volume. We are certain that no medical officer of health would ever regard untreated Thames water as bacteriologically safe to drink, and since swimming involves drinking it must follow that the river water is equally dangerous to bathe in.

Bland-Sutton Institute of Pathology, Middlesex Hospital, London, W.1. R. E. M. THOMPSON
D. B. LONGMORE.

TROLLEY-SETTING

SIR,—The provision of individual packs of dressings and instruments by central sterile supply departments makes it necessary and possible to modify the present practice of trolley-setting.

Bowls and gallipots are a nuisance to sterilise and their use is purely traditional and quite unnecessary. Dressings should be used straight out of the pack and should not be emptied into a bowl, and the use of gallipots for antiseptics and lotions can be avoided equally easily. There is no need to soak a swab in a gallipot full of spirit in order to clean the skin before an injection. A few drops delivered from a drop bottle on to the swab are equally effective. I do not advocate the use of sprays for this purpose, as I believe the mechanical rubbing action is more important than the chemical action of the antiseptic applied for a few seconds. For preoperative skin preparations, however, a spray is a most efficient instrument and will save swabs, antiseptics, gallipots, and time.

The pernicious custom of keeping fluids for injection in one of a row of unlabelled gallipots is now rarely seen, but one still hears of cases where spirit has been injected by mistake.

I believe there is no procedure which could not be improved by abandoning the use of bowls and gallipots, and their presence on a trolley is a sign of bad practice. Dressings should be used from individual packs, antiseptics from drop bottles or sprays, injections from ampoules or multi-dose containers—swabbed clean, not dipped into gallipots. Water and saline should be dispensed in small sterile bottles, which are used once only, and dirty dressings should be discarded into dispensable paper bags, not into bowls.

Can we persuade G.N.C. examiners to share this view?

Central Pathological Laboratory, Burnley, Lancs. G. BEHR.

LOCAN PESSARIES IN THE TREATMENT OF TRICHOMONAL VAGINITIS

SIR,—The findings of Dr. Eckersley and his colleagues (Sept. 3) accord with those in the Edinburgh special clinics.

Some time ago Dr. Murrell[1] referred to the number of cases in which local sensitivity to 'Locan' developed. In a further trial of the drug many patients complained of "intense vulvar heat"; and examination showed either severe vulvar œdema or an urticarial rash. One of my patients, in addition to the vulvar symptoms, had a rash on the fingers used to insert the pessaries; these side-effects subsided with discontinuation of the pessaries. This patient had no history of previous sensitivity to cocaine.

In view of these reactions, and because many other forms of local therapy are available, locan pessaries are not used in our clinics.

Special Clinic, Royal Infirmary, Edinburgh, 3. MARY SCOTT-GRAY.

DOCTORS, ADMINISTRATORS, AND THERAPEUTIC COMMUNITIES

SIR,—The excellent article by Dr. Crocket (Aug. 13) does, as subsequent correspondents have observed, point the way to reforms long overdue. But first clarification of the position of medical superintendents under the new Mental Health Act, which comes into operation on Nov. 1, is needed. To those who work in general hospitals it may seem incredible that the following points are still bones of contention:

1. The right of individual consultants to attend to correspondence about their own patients. From long usage letters are still often addressed to the medical superintendent and dealt with by him even though they concern another consultant's patients. This applies to all correspondence but especially that on legal matters.

2. The right of the consultant to know exactly which patients are under his charge. There are still spheres where some medical superintendents assume a sort of roving commission, especially in moving patients from ward to ward, "reviewing" them, and corresponding with their relatives.

3. The right to an equal share of new cases where no particular consultant is requested. Here again through custom, requests for admission, consultation (domiciliary or in clinics), and examination of prisoners and court cases are often addressed to the medical superintendent and are not shared. to a mental hospital only through the medical superintendent. Some general practitioners still think they can admit a patient In other words what corresponds to periods "on take" in general hospitals, whereby all consultants have a share of such cases, does not exist in some mental hospitals.

These are some of the basic problems which must be resolved if we are to put behind us the chronic dissatisfaction and frustration which has often existed in the past. There are, of course, many ways of doing this, among which are the following:

1. Negotiation in individual mental hospitals—probably the worst method.

1. Murrell, M. *Lancet*, 1957, ii, 1285.

2. Clear guidance from the Minister of Health.
3. A small committee composed of medical superintendents and consultants to examine the problem and submit their findings to wider opinion such as regional meetings of those concerned. This is the method I personally would favour.

Littlemore Hospital,
Littlemore,
Oxford.

J. E. DUFFIELD.

DOUBTFUL PROGRESS IN PSYCHIATRY

SIR,—Dr. Ahrenfeldt, in his letter last week, says that it is useless and also highly detrimental to the patient and society alike to make recommendations to a juvenile court which cannot in practice be implemented.

I myself prepare reports which give what I believe the court has requested—namely, my advice as a psychiatrist about the action to be taken in a particular case. If I find a child needing inpatient treatment I say so. I know that the pitiful number of psychiatric beds for children in London makes it unlikely that the child can be admitted. It is important that magistrates, probation officers, welfare workers, and officials should also discover this, so that pressure can be built up to remedy this state of affairs. It may be that we shall have to make do with placement in a residential school for the maladjusted, but even then it is better that all concerned know that it is a second-best and that the child needs something more.

Similarly, if I feel that an adult psychopath needs hospital treatment, I should say so. I know that the chances of securing his admission to the place of choice (perhaps the Henderson Hospital) are small, but as a physician I must state my patients' needs, as I see them. Failing to secure an admission, the court may have to decide to commit the person to prison, but it is surely important for them to see that what may be practical in social terms is not necessarily what is in the patient's interest.

I believe that, so long as psychiatrists confine themselves to making recommendations which fall within the present totally inadequate facilities, so long will this state of affairs persist, to the detriment of the individual, and of the society which at present cannot or will not make provision for the care and treatment which we believe is required.

London, S.W.5. W. H. ALLCHIN.

MYOCARDIAL INFARCTION DURING PREGNANCY AND PUERPERIUM

SIR,—I should like to comment on the interesting paper (Sept. 3) by Dr. Watson and his colleagues.

As they observe, serious atheroma is uncommon in women of childbearing age, and the youth of their patients is particularly striking. Thrombotic occlusion of a coronary artery is also rare in young pregnant women, and I believe that dissecting aneurysm should be considered as a possible cause of myocardial ischæmia in these cases.

Dissecting aneurysms primarily involving systemic arteries other than the aorta are certainly unusual, but have been reported with increasing frequency in recent years. In a report of 4 new cases in 1956, reference was made to only 15 acceptable cases in the earlier literature.[1] Since then more than 30 further cases have been reported—no less than 17 of them in one recent paper [2]—and a few additional cases have been unearthed from the literature. These various reports include a total of 9 well-documented cases with dissecting aneurysm of a coronary artery,[3–9] and it is notable that 2 of these were puerperal.[6 8]

A definite association is known to exist between pregnancy and dissecting aneurysm of the aorta,[10] and it may be that this holds for the coronary arteries also. The nature of this apparent association is quite unknown although in postpartum cases stresses induced by the physical exertion of delivery may be responsible; violent exertion was considered to be the cause of the 2 instances in soldiers reported by Uehlinger.[4] In all of these cases to which I have referred the diagnosis was made only at necropsy, but this reflects the difficulty of diagnosis rather than the inevitability of a fatal issue. Even at necropsy it is possible to mistake a dissecting aneurysm in a medium-sized or small artery for thrombotic occlusion on naked-eye examination.[1] It may be added that, in contrast to aortic dissecting aneurysm, occlusion of the lumen is much more common in these smaller vessels than external rupture.[1] Finally, the youth of the patients described by Watson et al. is more easily reconciled with a diagnosis of dissecting aneurysm than with coronary atheroma and thrombosis.

University Department of Pathology,
Western Infirmary,
Glasgow, W.1. A. J. WATSON.

1. Watson, A. J. *J. Path. Bact.* 1956, **72**, 439.
2. Foord, A. G., Lewis, R. D. *Arch. Path.* 1960, **68**, 533.
3. Glendy, R. E., Castleman, B., White, P. D. *Amer. Heart J.* 1937, **13**, 129.
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5. Hedinger, G. *Cardiologia*, 1947, **12**, 46.
6. Lovitt, W. V., Jr., Corzine, W. J., Jr. *Arch. Path.* 1952, **54**, 458.
7. Ahronheim, J. H., Wagman, G. F. *ibid.* 1959, **67**, 19.
8. Wells, A. L. *J. Path. Bact.* 1960, **79**, 404.
9. Boschetti, A. E., Levine, A. *Arch. intern. Med.* 1958, **102**, 562.

ACCURACY OF INJECTIONS FROM MULTIDOSE CONTAINERS

SIR,—The introduction of double-strength vaccines in 0·5 ml. doses increases the possibility that the error in the volume administered may sometimes be undesirably great.[11] To investigate this we invited 15 doctors in public-health work and general practice to inject alternately 0·5 ml. and 1·0 ml. water from a multidose container into a series of small rubber-capped vials, simulating as closely as possible their personal technique of inoculation.

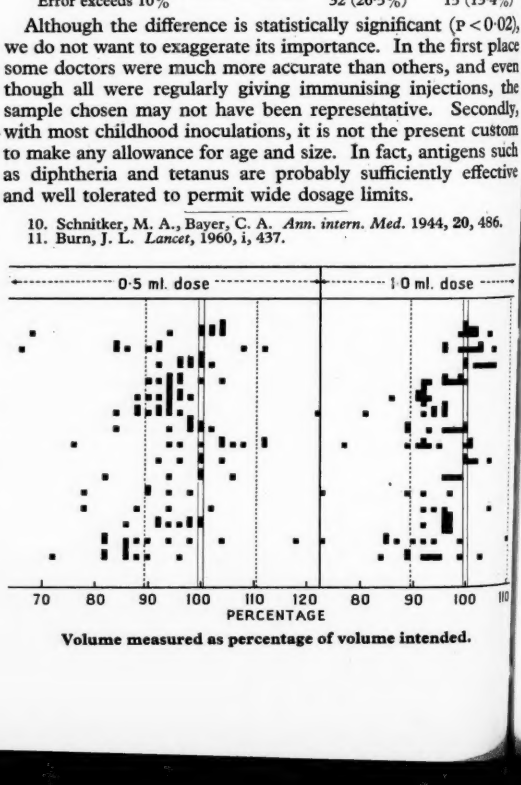
120 injections of 0·5 ml. nominal and 112 injections of 1·0 ml. nominal were returned and were accurately measured by reaspiration into a syringe graduated in divisions of 0·01 ml. This procedure was checked and found accurate to ±2%.

The results are shown in the accompanying figure. In 13·4% of 1·0 ml. doses and in 26·5% of 0·5 ml. doses the injected volume differs from the intended volume by more than 10% (this range is quite arbitrary).

	0·5 ml.	*1·0 ml.*
Total injections	120	112
Total below 90% of volume intended	27	15
Total above 110% of volume intended	5	0
Error exceeds 10%	32 (26·5%)	15 (13·4%)

Although the difference is statistically significant ($P < 0.02$), we do not want to exaggerate its importance. In the first place some doctors were much more accurate than others, and even though all were regularly giving immunising injections, the sample chosen may not have been representative. Secondly, with most childhood inoculations, it is not the present custom to make any allowance for age and size. In fact, antigens such as diphtheria and tetanus are probably sufficiently effective and well tolerated to permit wide dosage limits.

10. Schnitker, M. A., Bayer, C. A. *Ann. intern. Med.* 1944, **20**, 486.
11. Burn, J. L. *Lancet*, 1960, i, 437.



Volume measured as percentage of volume intended.

The limits with certain other antigens, however, including pertussis, are not so wide, and we think it is worth drawing attention to the increased likelihood of inaccurate and most commonly underdosage when smaller volumes are given in this way. It is desirable to use a 1·0 ml. syringe and to take particular care in measuring the volume. There is an obvious advantage in using ampoules in which single doses have been accurately measured by the manufacturer, although the cost is greater.

The majority of the doctors expressing a preference chose the 0·5 ml. dose. In a trial involving an individual follow-up of 144 babies we were not, however, able to demonstrate any real difference between the two types of triple antigen, either in the immediate response or in the reaction-rate during the first 48 hours.

We are grateful to our colleagues and to the health visitors who assisted in the investigations.

Greenford, Middlesex. T. B. BINNS.

Salford, Lancs. J. L. BURN.

CHROMOSOME ANALYSIS

SIR,—The method of chromosome analysis described by Bottura and Ferrari [1] and used by your contributors [2 3] does not seem clinically justifiable since it involves the administration of colchicine derivatives to patients.

It is known that colchicine causes heteroploidy and triploidy in animals, and its antimitotic properties are utilised in the treatment of patients with leukæmia. Since leukæmia may be associated with an abnormal karyotype there would seem to be a risk of causing leukæmia in healthy subjects by the use of antimitotic agents. The incidence of leukæmia is higher in mongols, who are heteroploid, and it would therefore seem especially hazardous to use antimitotics for diagnostic purposes in patients of suspected abnormal karyotype.

The intravenous administration of colchicine derivatives for diagnosis is unnecessary and potentially dangerous. Their use for this purpose seems clinically unacceptable and should be condemned.

Department of Surgery,
Queen's College,
Dundee. JOHN S. S. STEWART.

THE FEMALE PROSTATE

SIR,—When Mr. Moore published his article [4] I was quite impressed as I had worked on the same subject. When I read Mr. Skyrme Rees' letter (July 9) I was quite surprised that he denies the existence of periurethral glands (female prostate) in general.

When he states that prostatic carcinoma in the female is unknown in the animal kingdom, he is partially at fault. There are enough cases of carcinoma of the periurethral glands, which are the homologue of the male prostate. I was able to collect 41 reported cases with significant clinical and pathological data and added 3 cases of my own.[5] The literature on the embryology, anatomy, histology, and physiology of these glands is quite extensive and the fact that they exist has been well established. They respond to androgens in the same fashion as the male prostate. Mr. Moore, in his reply (July 23) to Mr. Rees' letter, says that it is not surprising that carcinomas of the female prostate do not occur because of the high œstrogenic environment.

I would like to point out that in analysing the literature I found that, of 44 collected cases, only 2 had occurred before the 5th decade. Therefore I concluded that adenocarcinoma of the female urethra (female prostate) is almost exclusively a disease of menopausal or postmenopausal women. It is quite possible that the high œstrogenic environment before the menopausal period does not permit the development of a carcinoma of the female prostate. During the menopause and after, when the œstrogen level falls rapidly and when the female prostate could respond to androgens from the adrenal glands, it is possible that an occasional carcinoma develops in these glands.

The carcinoma of the female prostate undoubtedly exists, though it is very rare. In my short practice of pathology, I was able to observe 4 such cases.

Wayne County General Hospital,
Eloise, Michigan, U.S.A. ROMAN KNOBLICH.

CATECHOLAMINE METABOLISM IN NEUROBLASTOMAS

SIR,—Study of catecholamine metabolism in association with phæochromocytomas has been extensive. These findings have proved most beneficial in diagnosis and follow-up care of such patients. However, few studies have been published regarding urinary excretion of noradrenaline, adrenaline, and 3-methoxy-4-hydroxymandelic acid (V.M.A.) in an embryologically related neural tumour, the neuroblastoma.

In 1957 Mason et al.[1] first reported increased urinary excretion of pressor amines in an infant with a neuroblastoma. Isaacs et al.,[2] Graham,[3] Stickler et al.,[4] and von Studnitz [5] have since recorded additional cases. Another possible case is referred to by Wilkins.[6]

Five infants and children with a tissue diagnosis of neuroblastoma have been investigated in our laboratory. Therapy in these patients consisted of surgery, intravenous nitrogen mustard, and/or radiation. Urinary excretion of noradrenaline and adrenaline was determined according to the method of von Euler and Floding.[7] Urinary V.M.A. was estimated using the method of Armstrong et al.[8]

Urinary Excretion in μg. per 24 hours

Patient	*Age*	*Before treatment*		*After treatment*	*Exacerbation*	*Normal value*
1	5½ yr.	Noradrenaline	53·7	15·3	69·6	<25
		V.M.A.	3625·0	2745·0	12,600·0	<2000
2	13 mos.	Noradrenaline	104·4	7·3	..	<15
		V.M.A.	1525·0	570·0	..	<1000
3	4 yr.	Noradrenaline	121·5	63·0	105·0	<25
		V.M.A.	1752·0	1100·0	1360·0	<2000
4	7 mos.	Noradrenaline	..	3·1	12·3	<15
		V.M.A.	..	500·0	690·0	<1000
5	7 wk.	Noradrenaline	14·7	..	13·4	<10
		V.M.A.	8000·0	..	28,750·0	<500

In patients 1 and 2 we found increased amounts of noradrenaline and V.M.A. before treatment. After treatment, the patients improved, and the values of these substances decreased. When patient 1 had exacerbation of his disease, the urinary excretion of noradrenaline and V.M.A. again increased. Patient 3 had increased excretion of noradrenaline before therapy; a clinical remission and decreased noradrenaline excretion after treatment; and increased noradrenaline excretion when the disease progressed. V.M.A. excretion remained normal throughout this time. Patient 4, who had severe generalised disease, excreted normal amounts of noradrenaline and V.M.A. in her urine during the course of her illness. Little or no benefit was derived from therapy, and the patient died within three months. Patient 5 had a slightly raised urinary noradrenaline, but a much elevated excretion of V.M.A. He, too, responded poorly to therapy and died within three weeks.

Urinary adrenaline was within the normal range in all cases.

These findings suggest that there is wide variation in the biochemical nature of these tumours. Alternate pathways for synthesis and metabolism of noradrenaline and adrenaline may be present. Serial determinations of the catecholamines and their metabolites seem to have

1. Bottura, C., Ferrari, I. *Nature, Lond.* 1960, **186**, 904.
2. De Assis, L. M., Epps, D. R., Bottura, C. *Lancet*, July 16, 1960, p. 129.
3. Leon, N., Ferrari, I., Bottura, C. *ibid.* Aug. 6, 1960, p. 319.
4. Moore, T. *Lancet*, 1960, i, 1305.
5. *Amer. J. Obstet. Gynec.* 1960, **80**, 353.
1. Mason, G. A., Hart-Mercer, J., Millar, E. J., Strang, L. B., Wynne, N. A. *Lancet*, 1957, ii, 322.
2. Isaacs, H., Medalie, M., Politzer, W. M. *Brit. med. J.* 1959, i, 401.
3. Graham, J. D. P. *Nature, Lond.* 1959, **183**, 1734.
4. Stickler, G. B., Hallenbeck, G. A., Flock, E. V. *Proc. Mayo Clin.* 1959, **34**, 548.
5. von Studnitz, W. *Scand. J. clin. Lab. Invest.* 1960, **12**, suppl. 48, p. 53.
6. Wilkins, L. The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. Springfield, Ill., 1957.
7. von Euler, U.S., Floding, I. *Scand. J. clin. Lab. Invest.* 1956, **8**, 288.
8. Armstrong, M. D., McMillan, A., Shaw, K. N. F. *Biochim. biophys. acta*, 1957, **25**, 422.

prognostic implications and to be useful in evaluating response to therapy. Studies of patients with neuroblastomas may permit a biochemical classification of these tumours in the near future.

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Upstate Medical Center,
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MARY L. VOORHESS
LYTT I. GARDNER.

PULSE-GIVING PUMP

SIR,—Your issue of April 30 contained an account of a new pulse-giving pump.[1]

I constructed a pump on this principle in 1948, and exhibited a working model at a combined meeting of the British Medical Association and the physiology department of the University of Melbourne in July, 1951. The project was discontinued owing to lack of financial support. I did, however, publish the essential principle of external compression by a piston.[2] Air was used instead of fluid as a compression medium, owing to constructional difficulties in a home-made device.

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Victoria, Australia.

R. F. BUTTERWORTH.

ZOLLINGER-ELLISON SYNDROME

SIR,—Our experience with case 2 of Verner and Morrison [3] leads us to agree that this syndrome indeed has many facets.

We observed this patient from the onset of his symptoms until his death 804 days later and are still groping toward a solution of the mystery of his disease. We were most struck by the prolonged abnormality of calcium metabolism, which was characterised by hypercalcæmia, hypophosphatæmia, and hypercalciuria. 33 serum-calcium determinations were made and of these 20 were greater than 10·5 mg. per 100 ml., the greatest being 16·5 mg. Before neck exploration, hypercalciuria was consistently present, daily urinary calciums being 469, 390, 382, and 320 mg. Following exploration on the 155th day after onset there was a marked decrease in calcium excretion except for the first postoperative day when 247 mg. was excreted. Thereafter the maximum obtained was 215 mg. on the 256th day; random 24-hour urine-calciums were 89, 124, 3, 23, 12, 27, 78, 11, 163, 155, 47, 40, 82, and 86 mg. On three separate occasions (days 224, 322, and 347) hypercalcæmia was accompanied by hyperphosphatæmia, azotæmia, and a decreased carbon-dioxide combining power. Serum-potassium was less than 3·5 mEq. per litre on 32 occasions, was normal 4 times, and was greater than 5 mEq. per litre only once. Despite the prolonged hypokalæmia the carbon-dioxide combining power was elevated (36 mEq. per litre) only once and was less than normal on 18 of 23 determinations. Partial balance study was done between days 632 and 638, and data relative to potassium intake and urinary excretion were as follows:

Day	*Diet*	*Intake (mEq.) supplement*	*Total*	*Urinary excretion (mEq. per litre)*	*Urine volume (litres)*
1	107	205	312	20·8	2·2
2	212	205	417	25·7	3·5
3	146	205	351	35·1	3·3
4	143	205	348	29·9	2·6
5	163	205	368	36·9	2·6
6	143	205	348	37·8	2·3
Total ..	914	1230	2144	186·2	

During the study diarrhœa was not a problem, and 3 of the 4 normal serum-potassium values obtained were within three weeks of the study. Potassium balance cannot be absolute because fæcal collections were not made, but serum-potassium at the beginning of the study was 2 mEq. per litre and twenty days later was 4·8 mEq. per litre. Serum-calcium at this time was normal.

These observations suggest an intermittently active tumour, but the mechanism by which changes were effected is unclear. The three episodes of hypercalcæmia, hyperphosphatæmia, and azotæmia suggest that the tumour may have elaborated a vitamin-D-like material which may have accelerated the absorption of calcium from the bowel, not unlike the mechanism thought to account for the hypercalcæmia of sarcoidosis.[4] The relation of hypercalcæmia to hypokalæmia is likewise unclear, although it has been demonstrated by stop-flow techniques that calcium infusion in dogs leads to increased urinary excretion of potassium.[5] Epstein [6] has also incriminated hypercalcæmia as a possible factor in producing hypokalæmia in man, probably by its action on the distal nephron. Data relative to calcium loading in humans are inconclusive, but calcium loading is rarely extended beyond eight hours. The absence of extensive renal calcification at necropsy quite possibly can be accounted for by the intermittency of hypercalcæmia; the presence of the typical lesions of kaliopenic nephropathy at necropsy does not exclude the role of calcium. Epstein et al.[7] in fact have demonstrated similar lesions in rats made hypercalcæmic by calciferol. We have recently observed hypokalæmia with hypercalcæmia in a patient with hyperparathyroidism due to hyperplasia and in another with multiple myeloma. Parathyroidectomy restored these values to normal in the first case while cortisone was effective in the second.

We have also observed another patient with hypercalcæmia and lymphosarcoma who on one occasion also had hyperphosphatæmia and azotæmia (blood-urea-nitrogen 88 mg. per 100 ml.). This patient, a middle-aged woman, had previously undergone nephrectomy because of pyelonephritis associated with cystinuria and stone formation. She was admitted initially because of unexplained fever and splenomegaly. Her initial daily urinary calcium excretions were 123, 114, and 118 mg. She was given sodium phytate and a low-calcium diet with a fall in her serum-calcium from 14·2 to 9·9. Her calcium excretion values during this period were 78, 56, 38, 8, and 58 mg. per day. After this therapy was stopped she on one day excreted 376 mg. calcium. Splenectomy was then performed and lymphosarcoma demonstrated. Her serum-calcium fell from 13·6 preoperatively to 11·5 mg. per 100 ml. and her urinary calcium excretion to about 200 mg. daily. However, with recurrence of her tumour, calcium excretion increased and reached 302 mg. on one occasion shortly before her death. These findings suggest that the tumour may have secreted a vitamin-D-like material and that such activity was partially counteracted by the action of sodium phytate.

This study was supported in part by a grant from the National Institutes of Health, Bethesda, Maryland.

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School of Medicine of
Wake Forest College,
Winston-Salem,
North Carolina.

JOHN H. FELTS
WILLIAM H. BOYCE
ROBERT W. PRICHARD.

STERILISATION OF THE DIABETIC'S SYRINGE

SIR,—Dr. Stephen Carter (Aug. 13) rightly calls attention to the great waste of time in sterilisation of the diabetic's syringe. One might also mention the problems of the diabetic when travelling away from home.

The recent availability of sterile disposable syringes with attached needles at a cost of less than 15 cents (U.S.A.) each (in 2 ml. sizes) has led me to supply some to diabetic patients, with instructions that immediately after injections they plunge the needle back into the rubber vial cap and store the syringe-needle-vial assembly thus, preferably in a refrigerator, until the next usage; discarding the syringe only when the vial is empty.

Department of Surgery,
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Detroit 7, Michigan, U.S.A.

SAM I. LERMAN.

1. Sørensen, A. H. *Lancet*, 1960, **i**, 959.
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6. Ferris, T. F., Levitin, H., Epstein, F. H. *J. clin. Invest.* 1960, **39**, 985.
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ARTIFICIAL INSEMINATION

SIR,—Concupiscence was necessarily part and parcel of adultery before the advent of A.I.D. With A.I.D., however, the question of concupiscence (defined as " lust ") does not arise. In reply to Dr. L. N. Jackson (Aug. 27), I cannot do better than quote from John P. Kenny, O.P.:

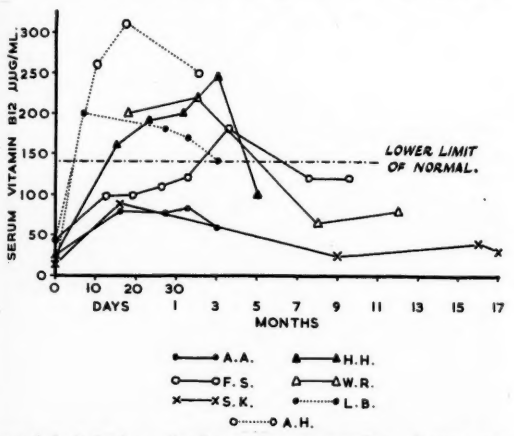
" The nature of the marital contract precludes a woman from receiving any seed except that of her husband. The right to propagate children is received in virtue of the marriage contract. This right belongs to husband and wife, and cannot be transferred to or used by a third party. If marriage rights were transferable, it would imply that the marriage bond itself is communicable." [1]

Hale, Cheshire. A. F. ROBERTS.

ORAL TREATMENT OF PERNICIOUS ANÆMIA WITH LOW DOSES OF H.P.P./1

SIR,—Dr. Mooney and Dr. Heathcote (Aug. 6) draw the conclusion that their vitamin-B_{12}-peptide complex is more potent in the oral treatment of pernicious anæmia than the equivalent amount of crystalline vitamin B_{12}. Unfortunately their observations do not decide whether this form of therapy is a good one.

We have investigated 10 patients treated with 'Distivit' (their peptide-vitamin-B_{12} complex). The accompanying figure shows the serum-vitamin-B_{12} levels of 7 patients thus



treated; in 3 the investigations were not complete. Assays were done by the *Euglena gracilis* var. bacillaris method of Ross. The doses used were one 100 μg. tablet t.d. for ten days, followed by one 100 μg. tablet once a day: in case S.K. the dosage was reduced to 20 μg. once a day after the first four months of treatment. The hæmatological responses, although slower than after parenteral treatment, were as a whole satisfactory. 1 of the patients, however, relapsed on 100 μg. daily maintenance dose, and the patient on 20 μg. doses in addition developed signs of subacute combined degeneration.

In 2 patients (A.A. and S.K.) the vitamin-B_{12} serum levels remained throughout pathological in spite of a hæmatological improvement, and in most of the others the levels decreased to subnormal or low values after three to eleven months of maintenance therapy.

It is absolutely essential to do serial vitamin-B_{12} serum estimations in all patients treated orally, say, every three months, whatever the form of oral preparation used (intrinsic factor + B_{12} or B_{12}-peptide complex), because the amount of vitamin B_{12} absorbed from the small gut appears to vary from case to case. Also it seems that after either type of oral preparation there may be some degree of inability to absorb satisfactory amounts of the vitamin.

1. Medical Ethics; p. 81. Cork, 1953.

Until such time as a safe commercial oral preparation, guaranteeing a satisfactory absorption of B_{12}, becomes available, oral B_{12} preparations should not be used in the treatment of pernicious anæmia. If, for some reason or other, oral treatment is preferred for *maintenance* therapy, periodic, say three-monthly, checks of the serum B_{12} level should be carried out.

City General Hospital, Sheffield. S. VARADI, A. ELWIS.

2-DIMETHYLAMINOETHANOL BITARTRATE (ATROL) IN DEPRESSIVE ILLNESSES AND CHRONIC SCHIZOPHRENIA

SIR,—The anti-depressive effects of 2-dimethylaminoethanol (deanol) bitartrate ('Atrol') have been studied in 45 patients, 20 of whom had depressive illnesses and 25 chronic schizophrenia. This letter gives an account of a clinical impression without the use of controls, and the dosage and duration of treatment were determined by day-to-day clinical progress.

Depressive Illnesses

The 20 patients with depressive illnesses were classified as follows: endogenous (including involutional) 13, manic depressive 1, neurotic depressive reaction 4, secondary to dementia 2. In the endogenous group none became worse, 9 were unchanged, 3 were slightly improved, and 1 showed a very good result.

Of the 9 endogenous depressives who were unchanged by treatment with atrol, all were severely ill, 5 were psychotic, and 3 were of long duration. The maximum daily doses which these 9 patients received were: 40 mg. (1), 60 mg. (1), 100 mg. (1), 120 mg. (3), 200 mg. (2), 400 mg. (1) (the only patient to whom the tablets were given in divided dosage, and only when the dose was raised above 200 mg. in one day).

Of the 3 who showed slight improvement, 1 had a maximum of 60 mg. daily and his improvement is only just being maintained with 20 mg. daily without maintenance electroconvulsive therapy (E.C.T.). The second, a chronic elderly depressive, is brighter and less generally retarded, and is being maintained on 100 mg. daily. The third is a man with a mixed depressive and paranoid psychosis, in whom the depressive component is alleviated by 200 mg. daily.

The very good result was in an elderly man with chronic depression who had been in hospital for thirty-three years; he improved markedly on 80 mg. per day, and is now being maintained on 40 mg. per day.

The manic-depressive patient was on the verge of depressive stupor, and his condition failed to respond to 200 mg. daily: he required E.C.T. for relief.

1 of the 4 people with neurotic depressive reactions showed a very good result, 2 were slightly improved, and 1 was unchanged. I am reluctant to attribute unreservedly these three improvements to the drug because of other factors.

A lady with severe dementia and a secondary retarded depression, when given 40 mg. daily, absconded from the ward, and on being brought back was belligerently resistive, until the effect wore off in two or three days. The second patient with depression secondary to dementia was unchanged.

No unwanted clinical side-effects occurred, and it is of interest that a man of 83 who was given 400 mg. daily without over-stimulation had previously been in what one can call a pre-convulsive state of hyper-reactivity from a normally therapeutic dosage of imipramine.[1]

My impression is that this drug is of little benefit in the treatment of severe endogenous depressions especially those with agitation, a viewpoint which is shared by Lemere and Lasater [2] and by Moriarty and Mebane.[3]

1. Levene, L. J., Lascelles, C. F. *Lancet*, 1959, ii, 675.
2. Lemere, F., Lasater, J. H. *Amer. J. Psychiat.* 1958, **114**, 655.
3. Moriarty, J. D., Mebane, J. C. *ibid.* 1959, **115**, 941.

The opposite view is expressed by Schorer and Lowinger [4] who recorded improvement in about one-fourth of psychiatric outpatients with depression treated for one month with deanol, and that improvement was greater in the psychotic than in the neurotic depressed patients.

Chronic Schizophrenia

The criterion for inclusion was mood depression and/or hypochondriasis within a diagnosis of chronic schizophrenia under treatment in hospital.

Atrol was given to 25 such patients, all males, as an adjunct to other treatments (occupational therapy, evening entertainments, weekend home leave in some cases, and phenothiazine derivatives). 11 patients were receiving chlopromazine, 7 perphenazine, 5 trifluoperazine, and 2 were on no tranquilliser.

Atrol was not given with the purpose of counteracting phenothiazine-induced drowsiness, a symptom which responds satisfactorily to the known anti-parkinsonian drugs such as trihexyphenidyl. 8 of the 23 patients having a phenothiazine derivative were in fact already having trihexyphenidyl as well.

The duration of treatment varied from six to thirty-four days. The maximum dosage ranged from 20 to 200 mg. in one day, given as a single after-breakfast dose.

3 patients had mild subjective relief of depression, 3 others became worse, expressing pre-existing bizarre ideas more floridly, and the remaining 19 patients were unchanged. No unwanted clinical side-effects were seen.

My impression is that atrol, in a varying dosage up to a maximum of 200 mg. in one day, has not been of significant help to these chronic schizophrenic patients showing depression and/or hypochondriasis. Other published results [5–7] have mostly been admitted to be inconclusive.

I am grateful to Dr. G. Fitzpatrick and Dr. C. F. Lascelles for their encouragement and permission to conduct this investigation, which was carried out at Cherry Knowle Hospital, Ryhope, Sunderland, to Dr. H. Merskey for his interest and advice throughout, and to Mrs. G. Swinhoe for clerical assistance.

I also wish to record my thanks to Dr. W. T. Simpson, of the research laboratories of Duncan, Flockhart & Co., for supplying the 'Atrol'. This product has now been withdrawn by the manufacturers. A different compound of the same deanol base is still being marketed by another firm.

Booth Hall Children's Hospital, Blackley, Manchester. LESLIE J. LEVENE.

THE CIRCULATING CANCER CELL

SIR,—In your leading article of Aug. 27 you say that "it is difficult to be sure that all the cells in the bloodstream which appear to be malignant are in fact so". This difficulty of identification is not a mere inconvenience leading to slight differences in the statistics from different centres. It is a major factor which should make one hesitate before accepting the statistics at all.

Searching for malignant cells is tedious and there is a tendency, especially if the diagnosis is known, to mark up dubious cells as "positive". A variety of large or immature cells can be found in white-cell concentrates from persons who have not got cancer, and these may occur in large numbers in patients who have. We have, for example, found various forms of megakaryocytes or their bare nuclei in nearly every specimen of 60 examined from both normal people and patients with benign disease. Cells which we believed to be malignant were found in only 7 out of 100 cases of malignant disease, and these 7 were all advanced cases with metastases.[8] Without doubt, cancer cells do get into the circulation in clinically operable cases, but probably not continuously enough to be demonstrable in small random samples.

If a worker claims to have found circulating cancer cells in operable cases without metastases, the onus should be on him to demonstrate the fact. Only one of the workers mentioned in your article has given some case-histories with illustrations of the relevant cells and follow-up data from a few specific "curable" cases.

The figures given in the literature should not be used to support a policy of giving cytotoxic drugs intravenously at the time of surgical operation, without a very thorough study of the morphological evidence from which the statistics have been compiled.

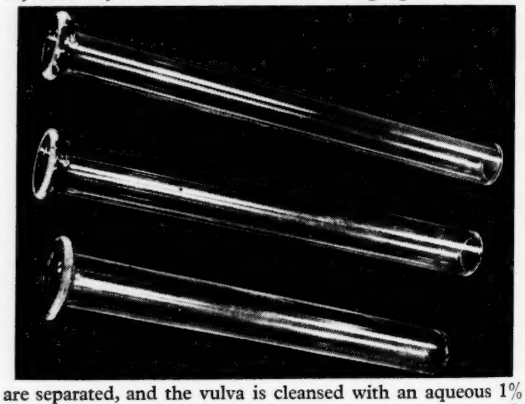
A. I. SPRIGGS
Churchill Hospital, Oxford. R. F. ALEXANDER.

COLLECTING MIDSTREAM URINE SPECIMENS FROM FEMALE PATIENTS

SIR,—The risk of infecting the urinary tract by routine catheterisation is widely known.[1] Catheterisation is, nevertheless, still commonly used to obtain a specimen of urine for laboratory examination and culture in female subjects. The reason is that the techniques of obtaining an uncontaminated midstream specimen (e.g., Hart and Magee [2]) are found by many nurses to be difficult, and because specimens so obtained often contain cellular debris from the vulva and yield contaminating organisms on culture.

Our purpose is to describe a new and simpler way of collecting an uncontaminated midstream urine specimen from female subjects. The method makes use of a glass tube approximately $^1/_2$ in. in diameter and 6 in. in length, one end of which is bell-shaped. The tube is made in various sizes (see figure).

To collect a urine specimen the subject sits on a low stool, or, if in bed, on a low bed stool with the legs apart. The labia



are separated, and the vulva is cleansed with an aqueous 1% solution of cetrimide and dried with sterile gauze. A sterile tube of appropriate size is chosen, the bell end placed in position over the urethral orifice, the tube held gently in position by the nurse, and the labia allowed to fall back over the tube. The patient then voids urine and the mid-portion of the specimen is collected in a sterile jar.

This method is simple and can easily be carried out by one operator; contamination of the specimen by contact with the labia is avoided; and it is possible to obtain specimens while menstruation is in progress.

It must be emphasised that a high proportion of uncontaminated specimens can be obtained without the use of a tube if due care is taken. Thus, in an experiment on 20 normal subjects carried out by one of us, 16 consecutive specimens were sterile without the use of the tube, and 20 out of 20 were sterile

4. Schorer, C. E., Lowinger, P. *Dis. Nerv. Syst.* 1959, **20**, 267.
5. Barsa, J. A., Saunders, J. C. *Amer. J. Psychiat.* 1959, **116**, 255.
6. Pennington, V. M. *ibid.* p. 165.
7. Toll, N. *ibid.* 1958, **115**, 366.
8. Spriggs, A. I. *Proc. R. Soc. Med.* 1960, **53**, 169.

1. *Lancet*, 1960, i, 1231.
2. Hart, E. L., Magee, M. J. *Amer. J. Nursing*, 1957, **57**, 1323.

when the tube was used. (The method of culture was to inoculate 1 loopful of urine on a blood-agar and a McConkey-agar plate. The possibility that the cetrimide solution used in cleansing the vulva might have affected the bacteriology of the urine was excluded by experiments in which urine so obtained was shown to have no inhibitory effect on small numbers of *Escherichia coli* and *Staphylococcus aureus* subsequently added to it [W. A. Gillespie, personal communication].) Because it is simple to use, however, and because it ensures no contact between urine and labia, it seemed probable that the routine use of the tube in the collection of midstream urine specimens would generally result in a higher proportion of uncontaminated specimens. This, in fact, has been our experience; 24 specimens have been collected from normal subjects by 5 student nurses and all were sterile on culture.

The prototype of this collection tube was made by the department of physics, University of Bristol. We wish to thank Mr. L. J. Waller, of the department of clinical pathology, Bristol Royal Infirmary, for bacteriological assistance.

Department of Medicine,
University of Bristol.

H. M. LEATHER
M. T. HUTCHINGS.

EFFECT OF ELECTROSHOCK ON SERUM-LIPOPROTEIN-CHOLESTEROL LEVELS

SIR,—Alterations in serum-lipids associated with electroshock therapy may be of considerable importance since coronary occlusion is a well-recognised hazard of such treatment [1–4]; but as yet the effects of electroshock therapy on serum-lipids are not clearly established.

van der Beek [5] observed small average increases in serum-cholesterol in a majority of patients after electronarcosis; and Bonati et al.[6] reported a slight lowering in serum-cholesterol levels after shock treatment. On the other hand, Kershbaum and coworkers [7] failed to demonstrate significant changes in serum-lipid concentrations in 14 subjects either as a result of anticipating electroconvulsion therapy or of the actual convulsion.

The effects of electroshock upon human serum-lipoprotein-cholesterol levels has not been reported. In order to study this serum-lipid fraction, blood was withdrawn from a group of 10 female psychiatric patients shortly before and immediately after electroshock therapy. Several of the women were subjected to repeated convulsive sessions. Serum-lipoproteins were separated electrophoretically on filter-paper and the amounts of cholesterol associated with the alpha and beta fractions were measured by the method of Searcy et al.[8] The first series of determinations performed on the sera from the 10 subjects indicated an apparent decrease in lipoprotein cholesterol following electroshock treatment. However, differences in cholesterol values were so small that the significance was questionable. Therefore, analyses for serum-lipoprotein-cholesterol were repeated on all serum samples in two separate laboratories using the same technique. These data were in close agreement, and showed the same trend as the initial determinations. The figures in the accompanying table are mean values of these replicate estimations.

It seems that following electroshock the distribution of cholesterol between alpha- and beta-lipoproteins was not much altered in the female patients studied. In no instance was the amount of total lipoprotein cholesterol significantly elevated after this type of therapy. On the other hand, a very slight but consistent depression in total cholesterol was observed in post-shock sera. Mann and White [9] have also reported small but consistent decreases in serum-total-cholesterol of experimental animals subjected to various stresses. These workers conclude that this reduction, apparently mediated through the adrenal gland, is a physiological response to stress.

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R. L. SEARCY
W. H. DAVIS
L. M. BERGQUIST.

1. Raskin, N., Johnson, R. S., Jr. *Dis. nerv. Syst.* 1951, **16**, 931.
2. Eyman, E. V., Morris, H. H. Jr. *Arch. Neurol. Psychiat.* 1950, **64**, 263.
3. Jetter, W. W. *ibid.* 1944, **51**, 557.
4. Sisler, J. C., Wilt, J. C. *Amer. J. Psychiat.* 1953, **110**, 354.
5. van der Beek, M. *Folia psychiatr. neerl.* 1955, **58**, 96.
6. Bonati, B., Salvi, A., Rancoti, J. B., Petrelli, M. *Folia Endocrin.* 1955, **8**, 321.
7. Kershbaum, A., Basset, D. R., Bellet, S. *Amer. J. med. Sci.* 1959, **237**, 341.
8. Searcy, R. L., Bergquist, L. M., Jung, R. C., Craig, R., Korotzer, J. *Clin. Chem.* (in the press).

SERUM-LIPOPROTEIN-CHOLESTEROL LEVELS BEFORE AND AFTER SHOCK THERAPY

Subject	Age (yr.)	Pre-shock cholesterol (mg. per 100 ml.)			Post-shock cholesterol (mg. per 100 ml.)		
		Alpha	Beta	Total	Alpha	Beta	Total
B.C.	33	74	221	295	61	177	238
		58	219	277	61	205	266
		63	181	244	61	174	235
		62	170	232	53	162	215
H.R.	58	75	274	349	69	246	315
		77	265	342	69	244	313
P.M.	33	91	191	282	76	180	256
		91	196	287	99	174	273
B.H.	41	90	232	322	71	219	290
H.P.	38	95	208	303	93	208	301
M.M.	31	57	132	189	55	129	184
M.L.	60	93	201	294	89	188	277
O.D.	44	95	242	337	109	208	317
H.D.	35	104	243	347	118	197	315
F.B.	72	72	199	271	73	200	273

Obituary

HAROLD DELF GILLIES

Kt, C.B.E., B.A. Cantab., F.R.C.S., Hon. F.A.C.S.

Sir Harold Gillies, who died in London on Sept. 10 at the age of 78, was consulting plastic surgeon to St. Bartholomew's Hospital, to the Ministries of Health and Pensions, and to the three Armed Forces. His surgical lifetime spanned two wars and he himself treated many civilians and Service men and women, casualties of peace and war. But not only his own patients owe a great deal to him. Patients of plastic surgical units all over the country are in his debt, for he was the creator of his specialty in this country and the teacher of two generations of plastic surgeons.

Universal Pictorial Press

He was born in Dunedin, New Zealand, in 1882, and he first achieved fame as an athlete. He rowed for Cambridge in 1904 and also played golf for the university. This skill he maintained, playing for England on a number of occasions up to 1926. He qualified from St. Bartholomew's Hospital in 1908 and took the F.R.C.S. two years later. His first interest was in ear, nose, and throat surgery.

Early in the 1914–18 war he joined the R.A.M.C. and he found himself confronted with large numbers of patients with appalling facial mutilations. He obtained permission to visit Paris to study with surgeons who were then among the leading European experts. Of this beginning W. K. F. writes:

"Gillies' mind was soon made up. He decided to start

9. Mann, G. V., White, H S. *Metabolism*, 1953, **2**, 47.

plastic surgery in the British Army. He got in touch with the War Office and came home from France, and with the help of Arbuthnot Lane and his own drive and personality by 1916 he was established as a specialist in plastic surgery at the Cambridge Hospital, Aldershot. At this time he knew little of his new subject, but his surgical experience, artistic temperament, endless patience, and boundless confidence carried him through. He loved his patients and inspired confidence in them. But he was still not satisfied. He wanted a hospital of his own. So he again approached Arbuthnot Lane and between them they persuaded the Red Cross to take over a large private house and grounds at Sidcup. A hutted hospital was built and became known as the Queen Mary's Hospital, Sidcup. There he was later joined by units from New Zealand, Canada, and Australia. In fact Sidcup was the East Grinstead of the first war."

It was during this time that Gillies independently discovered the potentialities and varied applications of the skin tubed pedicle. By 1920 he had established plastic surgery in Britain as a specialty and himself as its leading exponent. After the war, though he still doubted whether there would be enough plastic work in peacetime to give him a living, he set up in private practice. In due course he was appointed to the staff of Barts and of St. James' Hospital, Balham. It was at the latter hospital that he first met Mr. Rainsford Mowlem. Later they were joined by MacIndoe, and the famous "plastic" team was formed.

Between the wars Gillies' international reputation grew and he was an honoured guest in many countries. At home he played varied and important roles—as adviser to the Services and to the civilian authorities, and above all as a superb teacher and operator of the utmost distinction. At the beginning of the late war, with Sir William Kelsey Fry, he was asked to organise plastic surgical units for the treatment of jaw injuries, and he himself supervised the large unit at Park Prewett Hospital, Basingstoke. Soon after the war he helped to draw together the many surgeons of a younger generation who had recently entered plastic surgery, and to form the British Association of Plastic Surgeons. He also took an important part in planning the plastic surgery services in the National Health Service. He continued his work at Basingstoke until his 70th year, and until lately he was in private practice. His book, the *Principles and Art of Plastic Surgery*, written and illustrated by himself with Dr. Ralph Millard, which appeared in 1957, reflected his personality; for it was a classic exposition of the subject, yet both original and entertaining.

Gillies was knighted in 1930. He was also a commander of the Order of the Dannebrog and the Order of St. Olav. He was an honorary fellow of the Royal Society of Medicine and of the American College of Surgeons.

C. R. McL. writes:

"In 1953 Gillies' reception as the guest of the British Association of Plastic Surgeons was a memorable occasion worthy of his prodigious reputation as artist, golfer, motorist, oarsman, humorist—and surgeon. Despite increasing years, his flair for brilliant improvisations and startling innovations, whether in theory or practice, continued. There can be no doubt that this brilliant and versatile figure, with his questing mind and creative artistry, will always be regarded as the father of plastic surgery in this country."

By his first wife, Kathleen Margaret Jackson, Sir Harold Gillies had two sons and two daughters. After her death in 1957 he married Marjorie Clayton, who survives him.

MARJORY WINSOME WARREN

C.B.E., M.R.C.S.

IT is hard to believe that only some fourteen years ago Marjory Warren could recommend the creation of geriatrics as a specialty.[1] In fact she had already established herself as the earliest consultant in the proposed specialty. She was one of the first to appreciate that, as she put it, "the medical profession, having succeeded in prolonging the life of men and women, must no longer fail in its responsibility to the elderly when they fall sick or become infirm". By her work at the West Middlesex Hospital she accepted that responsibility and offered many elderly people renewed activity and independence.

She was educated at the North London Collegiate School, and after qualifying from the Royal Free Hospital in 1923 she held house-appointments at the Queen's Hospital for Children, Hackney, and clinical assistantships at the Royal Free Hospital and at the Elizabeth Garrett Anderson Hospital.

In 1926 she became an assistant medical officer at the West Middlesex Hospital in Isleworth. Nine years later, when the hospital took over the nearby poor-law infirmary, she was given the job of reorganising the care of several hundred chronic patients. Though the patients were kept scrupulously clean and tidy she was appalled by the lack of classification which hindered adequate treatment. "In the same ward were to be found senile dements, restless and noisy patients who required cot beds, incontinent patients, senile bed-ridden patients, elderly sick patients who were treatable, patients who were up and about all day, and unmarried mothers and infants." Her first act was to make a complete survey of all the patients, which showed that with adequate treatment many could leave hospital and return to their homes, and that even the incontinent and bedridden could be improved and given a fresh interest in life and some limited activity. Her methods were especially successful in the management of cerebrovascular disease in the elderly.

For many years she held the post of deputy medical director at the West Middlesex, and last year she was appointed C.B.E.

She was a founder member of the British Geriatric Society and was international secretary of the International Association of Gerontology. She spoke at many conferences abroad, and was on her way to give a paper at a meeting of the Medical Women's International Association at Baden-Baden when she met with a car accident. She died in hospital in Metz on Sept. 5 at the age of 62.

A. E. B. H. recalls that Dr. Warren was the newly elected president of the London Association of the Medical Women's Federation:

"I suppose the last function Marjory Warren attended in her new capacity was when she came to a lunch given ten days ago at the South London Hospital for Women to 20 Japanese women doctors. She had only just returned from a visit to California, where she had met a distinguished Japanese physician. At once she seized on this chance encounter to make our Japanese friends feel they were on ground which, though foreign, was to some extent familiar, and to a great extent friendly. Although only two of them spoke English, through those two she managed to carry her warm-hearted, spontaneous capacity for setting people at their ease. On the hospital authorities, who had never seen her before, she left an impression of a woman of outstanding personality. She was indeed a remarkable and charming person who will be deeply missed by her friends, her colleagues, and above all

1. *Lancet*, 1946, i, 841.

by the very great number of elderly patients (she would never refer to them as old) who owe so much to her imagination and constructive handling of their many problems."

A. L. W. writes:

"Marjory Warren was a discoverer in the true, scientific sense, in that she looked at something all of us had taken for granted for years and saw it in a completely new light. When a large group of the chronic sick was transferred to her care, she did not merely see a hopeless collection of human bodies, helpless, bedridden, apathetic, needing only devoted nursing and attendance to pressure points. She saw rather a group of patients—human beings needing medical care and treatment, the stimulation of movement, friendliness, and activity that gives life. With her intelligence and sound common sense she treated their disabilities, got them out of bed, mobilised their stiffened joints and taught us that incontinence in the aged is often more a matter of boredom and apathy than senility. She showed that hemiplegics could be taught to walk again, however old, and that families would willingly care for their old folk if these were rendered reasonably mobile and self-helping. At a time when acute hospitals were saying 'We can't do any more for her—send her to the infirmary', Marjory Warren was discovering for herself the principles of curative medicine for the elderly, and she may fairly be called the mother of geriatrics, though others have since added a scientific and sociological framework to the empirical basis she laid.

"To work with her was an experience, and at least one clinical assistant will not forget her brisk warm ward rounds with their careful insistence on accurate diagnosis, intensive nursing skills, and persistent unremitting exercise. Most of all, there is the memory of the cheerful word for each patient, the knowledge of their particular problem, and the respect for the dignity and individuality of each. Marjory was a delightful friend and companion, full of humour and warmth and vitality, shot through and through with wisdom and good sense. One never turned to her in vain for help or advice. Her tragic and premature death gives one a sense of outrage that so valuable and happy a life has been cut short; but perhaps the best reaction, and the one she would have wanted, is to give thanks for such a life of integrity, service, and friendship."

ALICE CAMPBELL ROSE

M.B. N.Z., M.R.C.P., D.A.

Dr. Alice Rose, anæsthetist to the London Chest Hospital, died on July 25.

She graduated in medicine in New Zealand in 1924, and after holding house-appointments in Dunedin she came to this country with a travelling scholarship. She was drawn to work among children, and while holding a house-appointment at the Infants Hospital in Vincent Square she met Dr. Kenneth Tallerman, whom she married in 1929. After her marriage she continued her work as a pædiatrician, and held appointments at several clinics, including the toddlers' clinic at Hammersmith Hospital, and was medical officer to a girls' school.

It seemed as though pædiatrics was to be her life's work, but at the beginning of the late war, in response to the need for anæsthetists, she turned to a new specialty. She quickly established herself in it, taking the D.A. in 1942, and joining the staff of the London Chest Hospital in 1945. Of her work there a colleague writes:

"To Alice Rose anæsthetics was not a routine occupation involving technical skill; it was an individual matter in which she made full use of her training as a physician. She was of the greatest help to many patients with social as well as medical problems, even though her official contact with them was the relatively remote one of an anæsthetist. She was a remarkably handsome and young-looking woman, and to her inherent friendliness and sympathy was added a measure of dignity and poise which nothing could disturb.

"In her home life she became Alice Tallerman, and she and her husband had many interests in common. Many friends were made free of the contented yet stimulating atmosphere that surrounded them. Their love of the countryside was given full play after the war when they settled in Essex, and those who visited them would never fail to be impressed by the serenity of their company."

Sir GORDON GORDON-TAYLOR

P. W. writes:

"Gordon-Taylor was perhaps the best loved surgeon in the world, loved by his patients, his pupils, his colleagues, and by the rising generation of surgeons throughout the Commonwealth. The men privileged to be appointed his registrar or house-surgeon had the best break of their lives. By his devotion to his patients, by his skill and his charm, he so impressed them with the best in surgery that the lesson could never be forgotten. And he did not lose interest when the period of apprenticeship was over but became a loyal friend, ever ready with help and encouragement. Those of his pupils who later achieved success, and they are many, owe a debt to G-T. that they can only acknowledge because it is too great ever to repay. And the legion of younger surgeons from Australia, Ghana, India, New Zealand, Pakistan, and many other countries to whom he devoted the later years of his life must add their names to the finest memorial a man can have —My spirit lives in you."

A Danish surgeon writes:

"To surgeons coming from other countries to study British surgery, Sir Gordon has been throughout his life a most appreciated adviser, always very helpful and friendly. With his knowledge of surgery and surgeons, his sound judgment of the problems of each particular man, he was able immediately to put one 'on the right track'. In every case he took a great interest in securing that one did not waste one's time.

"His scientific works on the surgery of the intestines, the parathyroids, carcinoma of the breast, and his hindquarter amputations were of the greatest interest and value to Scandinavian surgeons. They are and will probably always be of lasting importance as milestones in pre-war surgery.

"With his outstanding memory, his style in writing and speaking about his most extraordinary experiences by travelling to all the places where he was so well known and appreciated, he was able to entertain any surgeon of any age.

"All of us who have had the good fortune to meet and to listen to this 'Grand Old Man' will remember him all our lives and will be grateful for all he gave in help, instruction, and friendship. He was indeed a great surgeon and a good friend."

The British members of the International Society of Surgery, of which Sir Gordon was a vice-president, have received the following telegram from Prof. Paul Martin of Brussels, the secretary-general of the society:

"Deeply moved by the death of Sir Gordon Gordon-Taylor the officers of the Société Internationale de Chirurgie send you their appreciation for the devotion manifested by our most distinguished membre d'honneur to the purposes of our Society. Sir Gordon will live for ever in the hearts of our members."

Appointments

EDMUNDS, P. N., M.D., B.SC. Edin.: consultant bacteriologist, Fife district laboratory, Cameron Hospital, near Leven.

HUNTER, HENRY, M.B. Lond.: senior assistant psychiatrist, to be designated deputy medical superintendent, Balderton Hospital, near Newark.

OWEN, O. E., M.B. Edin., F.R.C.S.: consultant in general surgery, Bridgend General Hospital.

ROBERTSON, J. D., M.D. Edin., F.R.C.P.E., F.F.A.R.C.S., D.A.: consultant anæsthetist, Royal Infirmary, Edinburgh.

RYAN, SHEILA RUTH, M.B. Lpool, F.F.A.R.C.S., D.A., D.OBST.: assistant M.O., Middlesex County Council (Finchley and Hendon).

Notes and News

THE CONGO

IN the Congo,[1] according to Dr. J. S. McKenzie Pollock, W.H.O. senior representative, the greatest medical need following the exodus of European medical personnel is attention to the preventive services, in order to preserve earlier gains—notably in the control of insect-borne disease. Reports of many small, localised outbreaks of smallpox continue to come in. In some places, it seems, no vaccinations have been done in the past two years. The limiting factors in organising a vaccination service are lack of supervisory staff and lack of security in some areas. Some patients with leprosy are leaving institutions and returning to their villages because of the difficulty in maintaining food-supplies in the institutions. Mosquito-breeding is reported to have increased substantially, and the numbers of cases of malaria and filariasis are increasing.

W.H.O. is placing its recruitment service at the disposal of the Congolese Government in order to obtain medical staff. The aim is to staff the basic medical services on a scale of minimum requirement until Congolese doctors can gradually take over. Plans for training Congolese undergraduate medical students are well advanced; and a programme is being established for Congolese medical assistants to take courses overseas to enable them to qualify as doctors.

Medical teams from the following countries are in the Congo:

Red Cross and Red Crescent teams.—Czechoslavakia, Denmark, Finland, Japan, Holland, Poland, Canada (2), India, Pakistan, Australia (2), Greece, Norway, United Arab Republic, East Germany (3), Eire, Sweden, West Germany (2), Yugoslavia.

Government teams.—Ghana (3), Switzerland, Israel (3), U.S.S.R. (3).

REHABILITATION OF THE ARTHRITIC

AT the final meeting of the world congress of the International Society for the Welfare of Cripples, held in New York from Aug. 28 to Sept. 2 with Prof. Howard Rusk in the chair, it was announced that the society has been renamed the International Society for the Rehabilitation of the Disabled.

As regards rheumatism the activities of the congress showed the urgent need for cooperation between medical specialists, lay experts, and the patients, if the arthritic person is to get an opportunity to help in his own rehabilitation and remain or become again a useful member of the community.

Having previously formed world commissions on cerebral palsy, poliomyelitis, and paraplegia, the international society has for some years been considering the formation of a world commission on arthritis and rheumatism, through which information and experience could be exchanged. At a meeting held with representatives of the International League against Rheumatism and the American Rheumatism Society, it was felt that there was no immediate need for a world commission but that an advisory committee on arthritis should be formed. To organise this, a committee with Dr. Francis Bach and Dr. Ronald W. Lamont-Havers as co-chairmen will meet representatives of the International League against Rheumatism and discuss means by which the two bodies can cooperate closely. The social, vocational, and employment aspects of rheumatism are well represented in the society, which has affiliations in many countries, some of which are not yet represented in the league.

Royal College of Obstetricians and Gynæcologists

Mr. T. F. Corkill will deliver the William Meredith Fletcher Shaw lecture on Friday, Sept. 23, at 5 P.M., at the college, 27, Sussex Place, Regent's Park, London, N.W.1. His subject will be New Zealand's Debt to British Obstetrics. Tickets may be had from the secretary at the college.

Medical Protection Society

The annual general meeting of this society will be held on Wednesday, Oct. 5, at 3 P.M., at 50, Hallam Street, London, W.1.

1. See *Lancet*, Aug. 13, 1960, p. 358; *ibid.* Sept. 3, p. 555; *ibid.* Sept. 10, p. 607.

Faculty of Radiologists

This Faculty will hold a meeting in Cardiff on Saturday, Oct. 15. At a joint meeting of the diagnosis and therapy sections Prof. Harold Scarborough will speak on medical work in the Nigerian teaching hospital.

Medical World General Practice Conference

This conference will be held on Sunday, Oct. 23, in the Victoria Halls, Bloomsbury Square, London, W.C.1. Lord Taylor will give the opening address, and the subjects chosen for discussion are the future of health centres, training for general practice, appointments systems in general practice, and problems common to the pharmaceutical industry and general practitioners. Further particulars and tickets (21*s.*) may be had from the conference organiser, *Medical World*, 55, Russell Square, W.C.1.

Oliver Bird Trust

Dr. Albert Tyler of the California Institute of Technology will give the fourth Oliver Bird lecture on Monday, Sept. 26, at 5 P.M., at the London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1. He will speak on immunological approaches to fertility control.

University College Hospital Medical School

Postgraduate demonstrations will be held at the medical school, University Street, London, W.C.1, on Thursday and Friday, Oct. 27 and 28. The annual dinner will be held at the Savoy Hotel, Strand, W.C.2, on Oct. 28, at 8 P.M. Tickets for the dinner (36*s.*) may be had from the hon. secretary, Old Students' Association, at the hospital.

Professional Nurses and Midwives Conference and London Nursing Exhibition

This conference and exhibition will be held, under the auspices of the *Nursing Mirror*, from Oct. 10 to 14, at Seymour Hall, London, W.1. Details may be had from the organiser of the exhibition, Dorset House, Stamford Street, S.E.1.

Association of Medical Records Officers

This Association is to hold a regional conference in Brighton on Sept. 24. One of the speakers will be Dr. M. A. Heasman, of the General Register Office, who will give a lecture on findings of the hospital inpatient inquiry. Further particulars may be had from Mr. E. S. Beauchamp, Queen Mary's Hospital, Sidcup, Kent.

Royal Photographic Society of Great Britain

Medical Group.—This group will hold an exhibition of medical photography in the society's house, 16, Princes Gate, London, S.W.7, from Nov. 7 to 22. The exhibition will be opened by Sir Robert Platt, P.R.C.P., on Monday, the 7th, at 7 P.M.

Sir Ifor Evans will give the inaugural address of the Royal Free Hospital School of Medicine on Wednesday, Oct. 5, at 3 P.M., at the Senate House, London, W.C.1.

On Wednesday, Sept. 21, at 5.15 P.M., at the Royal Free Hospital, Gray's Inn Road, London, W.C.1, Dr. A. G. Bearn, of the Rockefeller Institute, New York, will speak on genetics in medicine.

A meeting of the Biochemical Society will be held in the department of biochemistry, University of Glasgow, on Sept. 29 and 30. The programme will include a colloquium on the biosynthesis of nucleic acids.

At a meeting of the Anglo-American Medical Society to be held at the university department of chemistry, Lensfield Road, Cambridge, on Wednesday, Oct. 5, at 8 P.M., Dr. Paul Wood will give a talk on recent advances in cardiology. Further particulars may be had from the hon. secretary of the society, Mr. A. J. Eden, Cedar Cottage, March Road, Wimblington, Cambs.

The Magsaysay award ($10,000) for public service at Manila has been given to Sir Henry Holland and his son, Dr. Ronald Holland.

The National Association for Mental Health have published the proceedings of their conference on *Mental Health at Home and Abroad*, held in London last March. Copies (5*s.* 6*d.* post free) may be had from the Association (Maurice Craig House, 39, Queen Anne Street, W.1).